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Race/Ethnicity as a Risk Factor of Mother to Child Transmission among HIV Infected Mothers

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Methods: Data-Linkage was conducted on all women HIV+ cases, who delivered a child during the time period and reported to the Nevada state HIV with the live birth registries. Demographic and social data, separated into black and Non-black groups, were analyzed using logistic regression techniques on HIV maternal transmission and prenatal risk factors such as smoking, alcohol and drug use, prenatal care and sexual orientation.

Results: From 1990 through 2005, 189 women living with HIV in Nevada gave birth. Of these mothers 58% were black, ten times higher than their population proportion and over seven times the percentage of black women in the HIV negative mother population. The estimated odds ratio of HIV maternal transmission risk factors for women increased significantly within the categories of income ratio, marital status, education and previous births, but remained approximately equal in the category of race/ethnicity. Odds ratios for HIV transmission also decreased significantly for women according to age.

Conclusions: Odds ratios of HIV risk factors occur highly disproportionate for certain demographic variables, but not for the race/ethnicity categories of black and Non-black women. Cross-match between health information systems may trace unresolved research questions.

Keywords

Cover Page Footnote

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Abstract

Objectives: African American women, living with HIV, exhibit a higher percentage of giving birth as compared to other race/ethnicity groups. The aim of this study is to understand the apparent black and non-black differences (health disparities) among the HIV Infected Mothers group and examine whether race/ethnicity can explain the high variation in different prenatal and HIV mother-to-child-transmission (MTCT) risk factors. Methods: Data-Linkage was conducted on all women HIV+ cases, who delivered a child during the time period and reported to the Nevada state HIV with the live birth registries. Demographic and social data, separated into black and Non-black groups, were analyzed using logistic regression techniques on HIV maternal transmission and prenatal risk factors such as smoking, alcohol and drug use, prenatal care and sexual orientation. Results: From 1990 through 2005, 189 women living with HIV in Nevada gave birth. Of these mothers 58% were black, ten times higher than their population proportion and over seven times the percentage of black women in the HIV negative mother population. The estimated odds ratio of HIV maternal transmission risk factors for women increased significantly within the categories of income ratio, marital status, education and previous births, but remained approximately equal in the category of race/ethnicity. Odds ratios for HIV transmission also decreased significantly for women according to age. Conclusions: Odds ratios of HIV risk factors occur highly disproportionate for certain demographic variables, but not for the race/ethnicity categories of black and Non-black women. Cross-match between health information systems may trace unresolved research questions.

**Key Words:** MTCT, HIV, Race and ethnicity, Linkage, Perinatal

INTRODUCTION

In the period from 1990-2005, an estimated 300,000 births in Nevada were reported to the Nevada State Health Division. Of these, approximately 251 children were delivered by mothers who were diagnosed before delivery with either HIV infection or AIDS disease. The race/ethnicity profile of these women indicated 58% were black, which is ten times higher than their population proportion, and over seven times the percentage of black women in the HIV negative mother population.

Black women accounted for the largest percentages of HIV/AIDS cases diagnosed women (67.2%) in the United States during 2001-2005[1]. Moreover, the largest percentage of children born to HIV/AIDS mother is also black mothers[2]. Moreover, health disparities reports have indicated higher HIV rates and increased risk factors for women of color[3-8] (Figure 1). These have also been investigated through analysis of youth risk behavior and adult behavioral risk surveillance data[9]. While population data indicate higher overall rates for black women compared to non-black women, analysis of risk factors by race/ethnicity has not been extensively examined[10]. Most previous studies that have been investigating mother to child transmission of HIV (MTCT) were centered on comparing and identifying socio-demographic and risk factors as predictors for the HIV+ mothers group as compared to the HIV negative mothers group, however, this study will examine the race role on MTCT risk factors among HIV infected mothers.

Maternal or perinatal transmission of HIV has decreased over the last decade due to effective anti-retroviral therapy administered before and during childbirth[11-13]. The decreasing trend of HIV maternal transmission is most evident after about 1999 when HIV anti-retrovirals (ARV) became widely available through the Ryan White Title II program[12], Medicaid and private insurers. Other risk factors such as drug and alcohol use, and insufficient prenatal care have been shown to impact HIV maternal transmission rates[11, 15-17].

We examined risk factors according to demographic categories, in addition to race/ethnicity for HIV positive mothers giving birth in Nevada during the period of 1990-2005 (Figure 1). Before 1990, there were no HIV mothers reported in Nevada.

Figure 1. HIV+ mothers as compared to HIV negative mothers in Nevada (NV 1990-2005)
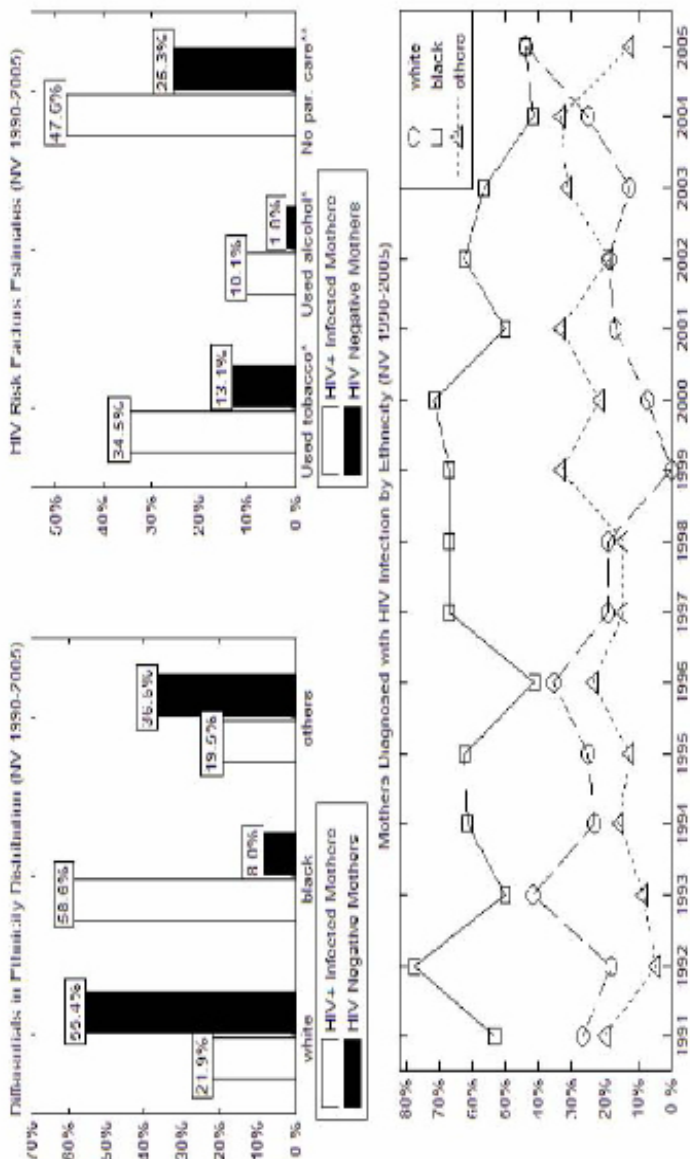
METHODS

All records in the Nevada HIV/AIDS Registry (HARS) and the Nevada Birth Registry for birth years 1990 through 2005 were included in this study. 1990 was the earliest year when Nevada HARS has been implemented. The records from two systems then were cross matched using a probabilistic record linkage algorithm (AUTOMATCH) software to obtain a list of all possible mother-infant pairs[18-20]. The matched pairs were identified based on the name, gender, race/ethnicity and social security number. Moreover, the matched pairs were further analyzed by quality control methods, using the SAS system, based on other demographic variables such as mother and child age, birth date, city, zip-code, and county to identify misclassified matched pairs[21]. By cross matching these two databases it was found that 437 children were born to 271 HIV infected mothers. However, for the objectives of this paper, only mothers who had been tested positive and diagnosed before or during pregnancy were considered (Figure 2).

Figure 2. HIV+ Mothers selection process of the HARS-Birth linkage (NV 1990-2005)
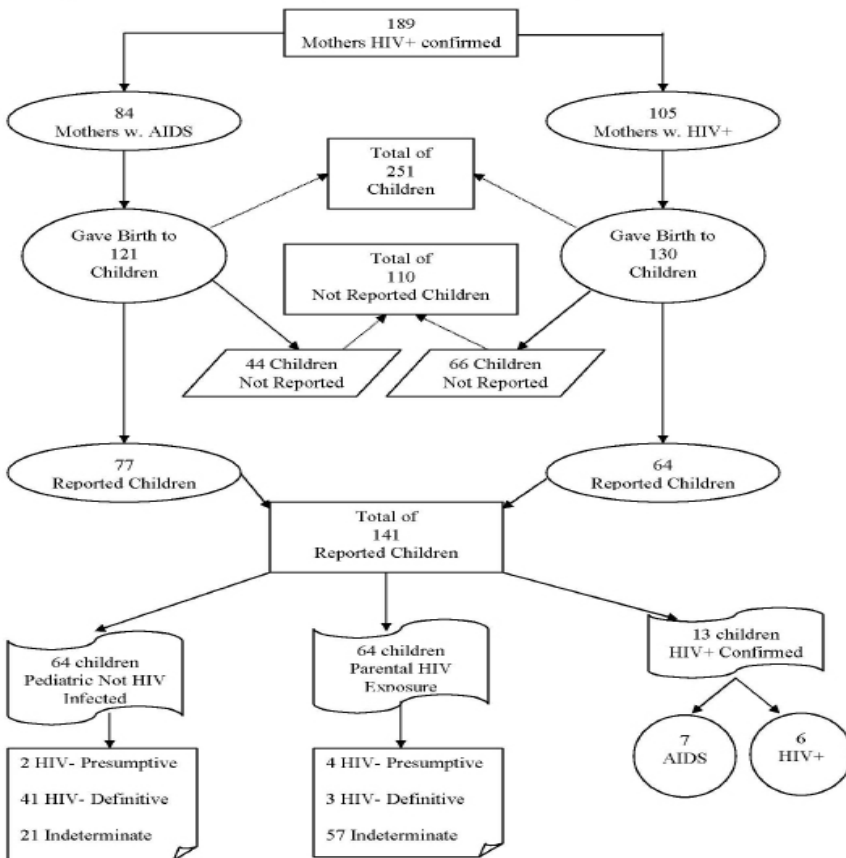
Race/ethnicity groups of mother defined in this study were White (Non-Hispanics), Black (Non-Hispanic), and Others. Considered cases were identified by both clinical (asymptomatic HIV infection, symptomatic HIV infection, and AIDS diagnosis) and laboratory results (four categories of CD4 counts). Unknown diagnoses for both categories accounted for 14 mothers (7.4%). Bridging[22] techniques were used to insure that matched pairs are exact with respect to race/ethnicity. However, since black mothers are impacted disproportionately to their numbers in the population, (8.0% of Nevada birth registry are black mothers who, on the other hand, make up 58% of Nevada HIV+ infected mothers (figure 1 left panel)), and since the percentage of black mothers infected with HIV didn't level down throughout the years 1990-2005 substantially (figure 1 bottom panel), White and the Others race/ethnicity categories therefore were combined for this study as non-black [23].

Demographic categories were compared using age, education, income level, marital status, and previous births. Five age groups were created (<20, 20-24, 25-29, 30-34, 35+). Educational level was assessed by completion of less than high school, high school, or more than high school. income level (area-based measures) was a comparison of household income to the median income level, either lower or higher, within the zip code of residence. Median household income of mothers' residence zip codes was obtained from the 2000 U. S. Census. Note that these are wide income averages, which provide only indirect evidence about the income[24]. Six cases in which zip codes could not be determined or differed in either registry, father and child information were used instead.

Marital status was defined as never-married or married at least once. The previous births category included none, or one or more. HIV transmission risk factors were assessed by smoking, alcohol and drug use during pregnancy, attending prenatal care within the first trimester, and sexual orientation[25-28].

Logistic regression was utilized to obtain the odds ratio of HIV transmission risk factors for each of the dichotomous demographic categories. A 95% confidence interval was also generated for each of the odds ratios. Significant odds ratios were indicated at the p<0.05 level (Table 2) and area under the ROC curve was estimated as a discrimination measure for the conducted multiple logistic models[29] (see statistical analysis and study limitations sections where goodness of fit and model accuracy measures are explained).

Following is the formula we used for the choice of the explanatory variables in which classifies the predictors into three categories.

$$\text{logit}\left(p_i\right) = a + b_1 E + \sum_{j=2}^{l} b_j V_{j,i} + \sum_{j=l+1}^{k} b_j W_{j,i}$$

Note that $i = 1,2,...,n$, represents the number of subjects, and P is the outcome, e.g. HIV+ or HIV-, while E, V and W denotes the Exposure, Potential Confounding, and Effective Modifiers variables respectively. In our study the Race/ethnicity group was treated as the "exposure" factor.

Study Limitations

An unavoidable statistical limitation of this study is the use of parametric methods while trying to measure the discrimination ability of the explanatory variables that have similar characteristics and the detection of relatively small changes. If our response, on the other hand, was binary as HIV+ versus HIV-, then this limitation would not exist. Non-linear methods could be used as an alternative such as the propensity score calculated based on distance measure. To make meaningful statistical inferences from the built models, only models with the accuracy measure AUC (area under ROC curve) greater than 0.60 were considered.

HIV/AIDS Reporting and Surveillance System (HARS) is a confidential patient reporting and data analysis system30 where cases are completed by health care providers and public health surveillance personnel for accurate and timely data. An important limitation of the HARS system is that some data may only be partial due to delayed reporting and lost to follow up cases. For example the date of First Positive HIV Test may not be representative to the actual date of diagnosis[31-32] and thereby some mothers were excluded from our study because their information was completed only after giving birth. Moreover, HARS does not include all persons diagnosed with HIV/AIDS in the United States, as it is designed to describe target populations and therefore the HARS-birth registry match cannot account for unreported maternal cases (Figure 2). In addition, it would be impossible to identify a match for a woman who gave a false identification to HARS for unexplained reasons.

Statistical Analysis

For the objectives of our study in order to examine whether race/ethnicity can explain the high variation in HIV risk factors in HIV infected mothers we considered only the HIV+ infected mother group for analysis. Before modeling, the SAS two sample TTEST procedure was performed (black vs. non-black mothers) which in turn conducts two tests. First is the t-test for equality of mean and secondly the F tests for equality of variance for the continuous variables: age (range: 13-42), number of years of education (range: 3-17), median income of income level ($20,000-$120,000), and previous births count (logarithmic transformation for previous births count was implemented to guarantee residual normality and variance consistency[33]). Dichotomies of the continuous variables along with the contingency tables were used as a separation method to select candidate indicators to enter the logistic models. Dichotomization didn't change the results of the TTEST when using the Rao-Scott Modified χ2 test[34] (table 1). In addition, the age variable was included in all models even though it didn't show any significant difference between

black and non-black mothers within the HIV+ group. Keeping the age variable in the models is epidemiological rather than statistical since it has been traditionally considered as a strong HIV+ confounding variable[35].

The use of logistic modeling to assess health data has been increasing in the recent years; however only a small percentage of researchers consider goodness of fit models [36-37].Multiple logistic regression was performed using the SAS logistic procedure to identify predictors on 3 binary HIV+ risk factors (smoking during pregnancy, alcohol use during pregnancy and no perinatal care in the 1st trimester) and one tri-response HIV+ factor (mode of exposure) respectively (table 2). For the binary risk factors the log odds function (with the LINK = LOGIT option) was used, however for the tri-response risk factor the generalized logit function (with the LINK = GLOGIT option) was used.

Table 1. Characteristics of Participants (N=251)

	HIV+ Infected Black Mothers			HIV+ Infected Non-Black Mothers			Equality of Distribution (chi-square)
	N	%	C.I.(95%)	N	%	C.I.(95%)	p
Total	147	58.6%	(52.5-64.7)	104	41.4%	(35.3-47.6)	<0.0001
Age <20	12	8.2%	(3.7-12.6)	3	2.9%	(0.0-6.1)	0.507
20-24	42	28.6%	(21.2-35.9)	29	27.9%	(19.2-36.6)	
25-29	38	25.9%	(18.7-33.0)	30	28.8%	(20.1-37.6)	
30-34	31	21.1%	(14.4-27.7)	23	22.1%	(14.1-30.1)	
35+	24	16.3%	(10.3-22.3)	19	18.3%	(10.8-25.7)	
Education Less Than H.S.	41	29.1%	(21.5-36.6)	45	45.5%	(35.6-55.3)	0.032
H.S or G.E.D.	72	51.1%	(42.8-59.4)	39	39.4%	(29.7-49.1)	
Post-H.S./Clg Grad	28	19.9%	(13.2-26.5)	15	15.2%	(8.0-22.3)	
Income Ratio Low Income	17	11.6%	(6.4-16.8)	13	12.5%	(6.1-18.9)	0.004
Middle Income	72	49.0%	(40.8-57.1)	30	28.8%	(20.1-37.6)	
High Income	58	39.5%	(31.5-47.4)	61	58.7%	(49.1-68.2)	
Marital Status Married	30	20.4%	(13.8-27.0)	32	30.8%	(21.8-39.7)	0.038
Never Married	72	49.0%	(40.8-57.1)	36	34.6%	(25.4-43.8)	
Divorced/Separated	3	2.0%	(0.0-4.3)	7	6.7%	(1.9-11.6)	
Unknown	42	28.6%	(21.2-35.9)	29	27.9%	(19.2-36.6)	
Previous Births None	29	20.1%	(13.5-26.7)	32	31.1%	(22.1-40.1)	0.018
1-2	62	43.1%	(34.9-51.2)	49	47.6%	(37.9-57.3)	
3+	53	36.8%	(28.9-44.7)	22	21.4%	(13.4-29.3)	

N: number of cases.   %: column percentage   C.I.: 95% confidence interval

Table 2. Socio-demographic measures and HIV+ risk factors associations, Multivariable Logistic Regression Analysis, HARS-Birth 1990-2005.

Socio demographics	Smoking during Pregnancy		Alcohol during Pregnancy		No Prenatal care in 1st trimester		IDU		Heterosexual	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Race/ethnicity										
Black	0.59	(0.31-1.08)	1.18	(0.47-3.17)	1.40	(0.76-2.59)	0.45	(0.19-1.07)	0.79	(0.39-1.61)
Non-Black	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Income ratio										
Low Income	2.32**	(1.28-4.29)	2.17	(0.86-5.94)	1.01	(0.54-1.87)	4.42**	(1.79-10.90)	1.42	(0.68-2.96)
High Income	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Marital Status										
Not-married	1.36	(0.66-2.88)	2.28	(0.65-11.40)	2.08*	(1.00-4.45)	1.98	(0.70-5.59)	1.17	(0.54-2.54)
Married	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Education										
Less than H.S.	1.10	(0.45-2.77)	1.02	(0.22-6.58)	4.07*	(1.58-11.39)	0.31	(0.09-1.08)	0.70	(0.26-1.88)
H.S. or G.E.D	1.20	(0.51-2.92)	1.90	(0.47-12.11)	3.39*	(1.36-9.21)	0.78	(0.23-2.57)	1.36	(0.53-3.51)
Post H.S.	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Previous Births										
One+	2.34*	(1.14-5.06)	1.92	(0.66-6.83)	2.78***	(1.36-5.90)	5.51**	(1.76-17.29)	1.36	(0.65-2.86)
None	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Age (unit=2 years)	0.93***	(0.90-0.96)	0.81***	(0.76-0.86)	0.94***	(0.91-0.97)	0.97	(0.92-1.01)	1.07***	(1.04-1.10)
Sample Size	235		235		220		238		238	
Area under the ROC curve	0.668		0.636		0.710		NA		NA	
Likelihood ratio (Null Hypoth.)	P < .0001		P < .0001		P < .0001		P < .0001			
Goodness of fit (Hos.-Lem.)	P=0.4863		p=0.1318		p=0.7219		P=0.4093 (Deviance)			

$*P < 0.05$, $**P < 0.01$, and $***P < .001$.

the response being tested[38]. Note that the area under the ROC curve for the multinomial model (tri-response) is not available for SAS logistic models with the LINK = GLOGIT option. For testing the Global Null Hypothesis: BETA=0, the likelihood ratio test was used to determine whether the parameters are collectively equal to zero or not. Finally, Wald confidence intervals for adjusted odds ratios were used to measure risk likelihood of HIV+ infection between predictors' categories.

RESULTS

From 1990 through 2005, 189 HIV positive women (of whom 89% were exact matches by social security number) accounted for 251 (75%) of approximately 300,000 births reported to the Nevada State Health Division (NSHD). Of these mothers, 84 (33%) were diagnosed with AIDS, and 105 (42%) were HIV positive. Of the children born to these mothers, 141 were reported to the NSHD, with 13 reporting a confirmed AIDS or HIV positive diagnosis. After grouping the mothers by race/ethnicity, 147 (58.6%) were black, 104 (41.4%) were non-black. In comparison, the percentage of HIV negative black mothers delivering in Nevada constituted only 8% of the total population. Further population characteristics of HIV mothers include: 86 (35.8%) mothers who did not finish high school, 108 (43%) who were never married, and 186 (75.3%) who had previous childbirths.

Differentials in the distribution of socio-demographic and socioeconomic characteristics by race/ethnicity within the HIV+ mothers group were analyzed. Findings (Table 1) include HIV+ mothers having the same age distribution regardless of their race/ethnicity, black mothers having more years of education than non-black mothers. Furthermore, the income ratio areas where black mothers reside have a lower average household income than non-black mothers, black mothers have higher previous births than non-black mothers, and black mothers are 1.81 (p<0.05) times more-likely to be never-married than non-black mothers.

When the demographic groups were analyzed for differences in risk factor odds ratios, significant findings were apparent in several categories including income ratio, marital status, education, and previous births, but never in race/ethnicity (Table 2). Odds ratios were inflated to (2.32 OR, C.I.=1.28-4.29) for low income mothers and (2.34 OR, C.I. =1.14-5.06) for mothers with one or more birth with respect to smoking during pregnancy. The lack of first trimester prenatal care incurred higher odds ratio in the never-married category (2.08 OR, C.I. =1.00-4.45), the high school or below categories, (3.39 OR, C.I. =1.36-5.42) and (4.07 OR, C.I. =1.58-11.39) respectively. In respects to injection drug use, low income (4.42 OR, C.I. =1.79-10.90) and previous birth (5.51 OR, C.I. =1.76-17.29) mothers experienced increased risk.

The odds ratios for all HIV transmission risk factors were not inflated in the analysis between race/ethnicity groups. There is no evidence that black women had a higher risk of reporting smoking, drug use, and lack of first

trimester prenatal care, than their white and other race/ethnicity mother counterparts.

Within the same analysis, age was seen as a protective factor in the risk of HIV transmission factors including smoking, alcohol use during pregnancy, and prenatal care. The findings of the logistic models support the hypothesis that differentials in socio-demographic and socioeconomic characteristics explain the high variation in HIV+ risk factors, but there is no association between them and race/ethnicity. Considering our findings, we can infer that race/ethnicity-related differentials in socio-demographic and socioeconomic characteristics could explain the apparent black and non-black differences found.

DISCUSSION

Race/ethnicity has been a concern in HIV prevention and treatment due to the appearance of health disparities in incidence rates, testing frequencies, access to treatment and morbidity rates[39]. Understanding the underlying factors for these data may lead to improved diagnostic and treatment opportunities. These health disparities data, however, may be confounded by other risk factors which are more pertinent than race/ethnicity. This research is attempting to identify other demographic classifications which have increased risk factors for HIV transmission, and may be more explanatory for the apparent over representation of black mothers in the HIV positive childbearing population. The proportion of HIV infected African American women of reproductive age in Nevada was 58% (Table 1) which is 1.4 times more than the other racial/ethnic groups in this study. The effects of such proportions should not influence the conclusions of this study since the logistic modeling accounts for their impacts.

The results from the descriptive analysis as shown in Table 1 of the socio-demographic characteristics indicated that there was a disparity in vertical HIV transmission to children born to African American women. These characteristics include education, marital status, income, and previous number of births. However, the significance of some of these disparities was washed out when controlling for the independent variables in the multiple logistic. Lower educational and income levels increase the risk factors associated with maternal HIV transmission, as well as smoking and drug use. While these factors may be associated to HIV transmission, race/ethnicity does not have a relationship with these increased risk factors.

This study contributes to the understanding of risk factors for maternal HIV transmission which are independent of race/ethnicity within the Nevada childbirth population. When risk factors such as smoking, drug use and inadequate prenatal care are evaluated, the study only found associations with age, income levels, marital status, educational level and childbirth history, but not race/ethnicity. Further research is needed to examine the rates of maternal HIV transmission dependent upon a mother's race/ethnicity.

Given that transmission rates are already low, the data may not, however, provide a large enough sample size for analysis.

The high rate of infection among blacks provides the stimulus for improving the existing HIV-prevention programs and implementing new and culturally appropriate HIV/AIDS strategies. Agencies including the Centers for Disease Control and Prevention (CDC), along with public health partners and community leaders, are announcing its Heightened National Response to the HIV/AIDS Crisis among African Americans to reduce the toll of this disease[40]. This response includes expanding the reach of prevention services; increasing opportunities for diagnosing and treating HIV; developing new, effective, prevention interventions, including behavioral, social, and structural interventions; and mobilizing broader action within communities to help change community perceptions about HIV/AIDS [41]. The descriptive analysis of our study (Figure 1 left panel) provides auxiliary evidence of the need for such response, however; defensible analysis of risk factors by race/ethnicity (Table 2) did not sufficiently articulate the CDC findings. Thus, further examination of clinical based studies should couple the CDC response within the African Americans community.

We end this paper elaborating on the striking finding of unreported 110 (43.8% of the total children born to mothers with HIV+) children in the HARS system. Given that the probability (within the HIV+ mothers group) of perinatal transmission in Nevada is about 9.3% (Figure 2), a new mechanism should be considered by policy makers so that unreported cases are researched and entered into the HIV/AIDS Reporting System (HARS) on a monthly basis. This mechanism is technical and should entail enhancing the HARS system by matching to other data sources such as the hospital discharge and birth registries. CDC has already modified HARS and it is now eHARS (Electronic HIV AIDS Reporting System); eHARS does contain the linkage function with the live birth registry[42], however this function is not relevant to the unreported cases to eHARS. The inclusion of birth history within this new enhanced system only required for the prenatal cases.

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