Title: Racial and Ethnic Disparities among Takotsubo Syndrome; A Nation-Wide Analysis

Abstract

Background: Takotsubo syndrome or cardiomyopathy (TTS) is a transient left ventricular dysfunction often precipitated by stress, with unclear mechanisms ranging from coronary artery spasm to microvascular dysfunction. Its true incidence remains uncertain, estimated at 1 to 2% among suspected acute coronary syndrome cases. This condition can have a favorable prognosis but is associated with fatal complications. Evidence suggests that TTS disproportionately affects minority racial groups due to elevated stress levels, highlighting the need for healthcare equity.

Aim: Our study focused on exploring racial and ethnic disparities in-hospital outcomes and clinical characteristics for patients diagnosed with TTS.

Results: In our analysis of 32,785 TTS hospitalizations, racial and ethnic disparities were significant: 80.5% were White, 6.7% Black, and 5.8% Hispanic, with the remainder from other minorities. Black and Hispanic patients, averaging 63 years, were younger than the 67-year average, with most below the 50th percentile of income, the majority being Black patients (50%). Black patients experienced more extended hospital stays (mean 4.5 days, $p < 0.001$) compared to Whites (3.4 days, mean decrease 1.1 days, $p = 0.002$), and Native Americans had the longest stays (5.1 days, mean increase 1.75 days, $p = 0.045$). Asian patients faced the highest healthcare charges (mean $79,111, increase $23,542, $p < 0.02$). Blacks had the highest risk of Diastolic Heart failure with 5.3% of patients (OR 1.6, $p = 0.03$). Cardiogenic shock with 8.25% in Black patients (OR 1.34, $p < 0.001$) and 11% in Asians (OR 2, $p < 0.001$). Blacks had the highest risk of stroke (4.8%, OR 2.1, $p = 0.003$). Pulmonary embolism in Blacks was (OR 1.8, p-value <0.001). Disparities extended to inpatient mortality and cardiac arrest, with Asians and Blacks facing the highest risks (1.8% mortality in Asians, OR 1.97, $p < 0.001$; cardiac arrest in Blacks 3.9%, OR 2.3, $p = 0.002$) compared to Whites.

Conclusion: Our findings reveal significant racial and ethnic disparities in TTS hospitalizations, with minority groups experiencing adverse outcomes and higher healthcare costs. These disparities underscore the need for targeted healthcare interventions and further research to understand and address the barriers to equitable care for TTS patients.

Introduction

Takotsubo syndrome or cardiomyopathy (TTS), first described in Japan in 1990, manifests as transient left ventricular dysfunction triggered by emotional or physical stress, resembling a "Takotsubo" octopus trap [1]. This condition predominantly affects postmenopausal women and mimics heart attack symptoms, though it occurs without coronary artery obstruction[1,2]. The underlying mechanisms of TTS are not fully understood. However, proposed theories include stress-induced increases in catecholamines, microvascular dysfunction, inflammation, estrogen deficiency, coronary vessel spasms, and myocardial stunning without obstructive coronary artery disease [3]. TTS can have a favorable prognosis but can be associated with fatal complications [2]. The real incidence of TTS remains unclear. It makes up for 1 to 2% of patients suspected of having acute coronary syndrome[3].

TTS cardiomyopathy demonstrates an evident correlation with physical stressors (36%) more than emotional stressors (27.7%) [6]. While studies have elucidated various aspects of this syndrome, there remains a paucity of research investigating potential racial and ethnic disparities among affected patients. Understanding such disparities is essential for optimizing patient care and treatment strategies and addressing healthcare inequities.

Our study focused on exploring racial and ethnic disparities in-hospital outcomes for patients diagnosed with Takotsubo Cardiomyopathy (TTS). Through a systematic analysis that included patient demographics and hospitalization metrics such as length of stay and total charges, clinical outcomes, and mortality rates, we offer a comprehensive view of the disparities within the healthcare system.

Methods

Using the National Inpatient Sample (NIS) Database Registry, we analyzed data from recent years 2017 to 2020.

Database

The National Inpatient Sample (NIS) is part of the Healthcare Cost and Utilization Project (HCUP) and is maintained by the Agency for Healthcare Research and Quality (AHRQ) [4]. The NIS contains information on all inpatient stays (not individual patients) in 48 states plus the District of Columbia, representing approximately 98% of the United States population, excluding rehabilitation and long-term acute care hospitals [4]. Unweighted, it contains data from more than 7 million hospital stays each year, and weighted, it estimates more than 35 million hospitalizations nationally [4] observations in the NIS contain a primary diagnosis, up to 39 secondary diagnoses, and up to 25 procedure codes, depending on the year [4]. All discharge diagnoses were identified using the International Classification of Diseases, 10th edition (ICD-10) codes [5]. The AHRQ made these data available to the principal author via the HCUP.

Statistical Analysis

National estimates were obtained using the discharge-level weight variable (DISCWT) provided by the HCUP. Weighted data were used for all statistical analyses. Missing values were excluded from the analysis. Categorical variables were compared using the Chi-square test and are described using frequency with percentages. Continuous variables were compared using the student's t-test and are reported as mean (±SD) if their distribution was normal or compared using the Mann–Whitney U test and reported as median (interquartile range [IQR]) if their distribution was skewed. Multivariate linear and logistic regression was used to compare hospital outcomes between groups, adjusting for potential confounders, which included age,

Charlson comorbidity index, hospital bed size, teaching status, and insurance. Statistical analysis was performed using Stata version 18 (Stata Corp, College State, Texas). A p-value ≤ 0.05 was considered to indicate statistical significance for all analyses. Variables used in the regression model building were either selected from the dataset as provided variables or abstracted with the ICD-10 codes.

Inclusion criteria and study variables.

The study cohort consisted of all hospitalizations among individuals categorized as either white, Hispanic, Black, Asian, Native American Indian, and other races. Patients who had missing race or reported other race/ethnicity were included as others. We extracted the following independent variables: sociodemographic characteristics (including sex, age, mean annual income in zip code, and insurance type), hospital characteristics, comorbidities, Charlson comorbidity index, and outcomes (Tables 1 and 2). We used ICD-10 codes to identify principal/secondary diagnoses (Supplemental table). To investigate disparities, we studied baseline characteristics and outcomes for TTS hospitalizations among all races (Supplementary Table 1).

Results

Patient Demographics and Hospital Metrics:

Among 32,785 hospitalizations with a principal diagnosis of TTS, demographic distributions were as follows: White patients comprised 26,395 (80.5%), Black patients 2,155 (6.7%), Hispanic patients 1,865 (5.8%), Native American Indians 175 (0.5%), Asian patients 555 (1.7%), and others 725 (2.2%). The average age was 67, with 89.4% of patients being female. However, among Black and Hispanic patients, the average age was 63. The primary hospital location was in the Southern region for 50% of the Black patient population, 32.15% of White patients, and 43% of Hispanic patients, compared to 48% of Native American Indians and 61.2% of Asian patient populations in the Midwest. Most patients were below the 50th percentile of income: 50% of Black patients, 38% of Native American Indians, and 32% of Hispanic patients were in the 0-25th percentile, compared to 52% of White patients and 66% of Asian patients, which were above the 50th percentile (Table 1 and Figure 1).

Length of Stay (LOS) and Total Charges (TOTCHG):

The mean length of stay (LOS) among patients with TTS was 3.5 days. Black patients had a mean LOS of 4.5 days with a mean increase of 1.1 days (p-value <0.001, 95% CI 0.6 to 2.5), and Native American Indian patients had a mean LOS of 5.1 days with an increase of 1.75 days (p-value 0.045 95% CI 0.3-3.5), compared to LOS of 3.5 days for White patients with a mean decrease of 1.1 days (p-value 0.002, 95% CI -1.6 to -0.5). However, Asian patients had a mean LOS of 3.8 days with an increase of 0.4 days (p-value 0.17), and Hispanic patients had a mean LOS of 3.3 days (p-value 0.9), others with 3.5 LOS (p-value), which were not statistically significant. (Tables 1 and 3)

The mean total charge (TOTCHG) among patients with TTS was $55569. Black patients faced a mean TOTCHG of $65,635, with a mean increase of $12,019 (p = 0.02, 95% CI 1,785-22,252). Hispanic patients had a mean TOTCHG of $71,443, with a mean increase of $15,874 (p = 0.002, 95% CI 5,497-25,364). The highest mean TOTCHG was noted for Asian patients at $79,111, an increase of $23,542 (p < 0.02, 95% CI 3,377-42,339). Patients categorized as other races had a mean TOTCHG of $71,272, with an increase of $15,703 (p < 0.02, 95% CI 3,377-35,939). Conversely, Native American Indians and White patients had mean TOTCHGs of $71,234 and $53,042, respectively. Notably, White patients experienced a decrease of $14,442 from the mean (p < 0.001, 95% CI -23,931 to -4,954). (Tables 1 and 3)

Diastolic Heart Failure and Cardiogenic Shock:
Diastolic Heart Failure rates were 3.4% among White patients (OR p-value 0.026 95% CI 0.6 0.41- 0.94) Native Americans was 2.2% (OR 0.7, p-value 0.68) and Hispanic was 4% (OR 1.2, p-value 0.49), Asians 0.8% (0.2, p-value 0.13) compared to 5.3% among Black patients (OR 1.6, p-value 0.03, 95% CI 10.6 to 2.42).
Cardiogenic shock was reported in 8.25% of Black patients (OR 1.34, p-value <0.001, 95% CI 1.16 to 1.56), 8.8% of Hispanic patients (OR 1.4, p-value <0.001, 95% CI 1.2 to 1.7), and 11% of Asian patients (OR 2, p-value <0.001, 95% CI 1.5 to 2.5), compared with Native American Indian patients at 8.59% (p-value 0.172), other races at 7.6% (p-value 0.121), and White patients at 6.3% (OR 0.7, p-value <0.001, 95% CI 0.6 to 0.8). Ventricular arrhythmia was only associated with the Black population at 5.8% (OR 1.2, p-value 0.041, 95% CI 1.1 to 1.3) while other races were not statistically significant.
Pulmonary Embolism and Stroke:
Stroke prevalence was 4.8% among Black patients (OR 2.1, p-value 0.003, 95% CI 1.2 to 3.4) and 4.14% among other races (p-value <0.001), with Native American Indian patients at 5.7% (p-value 0.218), Asian patients at 1.8% (p-value 0.776), and Hispanic patients at 2.68% (p-value 0.720) compared to 2.39% among White patients (OR 0.4, p-value 0.003, 95% CI 0.3 to 0.7). Pulmonary embolism was significant in 2.5% of Black patients (OR 1.8, p-value <0.001, 95% CI 1.4 to 2.4), other at 3.7% (OR 2.76, p-value <0.001, 95% CI 1.8-4.2), compared to 1.7% of Hispanic (p-value 0.227), 0.6% for Asian (p-value 0.094), 1% for Native American Indian (p-value 0.665), and 1.4% for White patients (OR 0.53, p-value <0.001, 95% CI 0.4-0.7).
Mortality and Cardiac Arrest:
Inpatient mortality was 1.8% for Asian patients (OR 1.97, p-value <0.001, 95% CI 1.5 to 2.5), 0.5% for Hispanic patients (OR 1.38, p-value <0.001, 95% CI 1.17 to 1.63), 4.14% for other races (OR 1.8, p-value <0.001, 95% CI 1.6 to 2.1), and 2% for Black patients (OR 1.5, p-value <0.001, 95% CI 1.3 to 1.7) compared to 1.5% for White patients (OR 0.7, p-value <0.001, 95% CI 0.6 to 0.8) and Native American Indians (p-value 0.465). Cardiac arrest was 3.9% in the Black population (OR 2.3, p-value 0.002, 95% CI 1.7 to 3.9), 2.1% for Hispanic (p-value 0.720), 3.6% for Asian (p-value 0.776), for Native American Indians (p-value 0.218), and for other (p-value 0.183) compared to 1.7% for White patients (OR 0.43, p-value 0.002, 95% CI 0.3 to 0.6). Outcome data for all races are presented in Tables 2 and 3.

Discussion

We analyzed the national inpatient sample and noted potential disparities in patient characteristics and clinical outcomes among different racial and ethnic groups hospitalized with TTS (Figure 2).

We found that most TTS hospitalizations were among White patients, with Black, Hispanic, Native American Indians, and other minority groups making up a smaller portion of the total patient population. The average age was 67, and females accounted for 89% of the cases, aligning with existing research data [6]. Our analysis also revealed that Black and Hispanic patients were, on average, younger at hospitalization (age 63), suggesting potential disparities in disease manifestation or healthcare access. Notably, 50% of the Black population with TTS fell within the lowest income quartile (0-25th percentile) (Figure 1). In our analysis, a notable distinction emerged within the Asian patient cohort affected by TTS, where 67.3% were identified in the higher income quartiles, particularly above the 51st percentile, indicating a majority within a high-income bracket.; the MASALA study explains that South Asian immigrants in the United States, have higher incomes largely due to selective immigration policies that favored professionals and those in demanded occupations, leading to a higher

socioeconomic status. Despite higher socioeconomic status, they face an elevated risk of cardiovascular disease due to genetic predispositions, including higher levels of lipoprotein(a), which are associated with an increased risk of heart disease [7].

There were significant disparities in the length of hospital stays and hospital charges. Black and Native American patients experienced longer hospitalizations, a 2–3-day increase compared to the average. Asian patients encountered the highest total charges, while both Blacks and Hispanics incurred higher costs than their White counterparts (Figure 3).

These differences could reflect greater severity of disease presentation, delays in receiving care, or biases within healthcare facilities. The increased financial burden on Black and Hispanic patients highlights the urgent need for policy changes to ensure equitable healthcare costs.

Our findings indicated that Black, Asian, Hispanics, and Native American patients were associated with a higher prevalence of comorbidities (Figure 4). Asian had the highest rate of cardiogenic shock followed by Black patients, who also experienced highest risk of Diastolic heart failure and ventricular arrhythmia.
This phenomenon may be attributed to significant disparities in cardiac care for Black individuals, encompassing prevention, invasive treatments, and outcomes [8,9]. Notably, Black patients often face longer delays in receiving medications, undergoing revascularization, and obtaining surgical treatments for acute coronary syndrome, including extended door-to-balloon times [9]. Genetic factors, such as the presence of the APOL1 and ADRB2 16R alleles in Black populations, might also play a crucial role in prompting worse outcomes [10,11]. The etiology of cardiogenic shock appears to be multifactorial, suggesting a potential link between cardiogenic shock and other major cardiovascular complications prevalent among Black and Asian patients [7,12, 13, 14].

Pulmonary embolism was notably higher in Black patients (OR 1.8, p-value <0.001) and patients of other races (OR 2.3, p-value <0.001) compared to other populations. Stroke prevalence was the highest at 4.8% among Black hospitalized patients (OR 2.1, p-value 0.003) and 4.14% among other races (OR 1.7 p-value <0.001), significantly higher than in other races. In contrast, White patients showed no significant association (OR 0.4, p-value 0.003) with stroke. These outcomes suggest disparities may stem from underlying health conditions, differential access to preventative care, or variability in care standards.

Mortality Rates:
Disparities in mortality rates were evident, with the highest inpatient risk of mortality observed in Asian (OR 1.97, p <0.001) and other race populations (OR 1.8, p <0.001), followed by 2% of Black patients (OR 1.5, p <0.001). Black patients also demonstrated a notable association with cardiac arrests (OR 2.3, p-value 0.002) compared to White patients, who showed no significant mortality association (OR 0.6, p <0.001).

In summary, it was noted that the Black population had more adverse outcomes compared to other races, which is consistent with literature [15].

Additionally, there is a hypothesis that chronic medical and socioeconomic stressors, which disproportionately affect specific minority racial groups such as Black communities, may influence the severity of Takotsubo syndrome outcomes [16]. It is proposed that the worse outcomes observed in these populations could be partially explained by elevated levels of

chronic stress, potentially leading to increased catecholamine production [1]. This hypothesis is supported by existing research indicating that the convergence of medical and socioeconomic challenges is more prevalent in certain minority groups and may significantly contribute to the pathophysiology of Takotsubo cardiomyopathy [16,1].

This finding underscores the importance of addressing social determinants, such as occupational factors, in understanding and mitigating health disparities.

Limitations:
The study faced several limitations. The reliance on an administrative database dependent on ICD10-CM codes, where incorrect coding could influence findings, was a primary concern. The lack of randomization was addressed using univariate and multivariate analysis. The strength of our study lies in the power of the sample size; we utilized a large population database, thus improving the validity of our findings.

Conclusion

This study sheds light on significant racial and ethnic disparities in outcomes for Takotsubo Syndrome (TTS). Despite TTS's higher prevalence among White patients, patients from Black, Asian, and other racial and ethnic backgrounds face a greater risk of severe conditions, such as pulmonary embolism, and higher mortality rates, especially among Black patients. These findings underscore the critical impact of socioeconomic factors and healthcare access on patient outcomes, suggesting that disparities in these areas may contribute to delayed diagnosis, treatment, and increased complications.

Further research and interventions are needed to address these disparities, focusing on understading and overcoming the socioeconomic and healthcare barriers that minority groups face.

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Patient Characteristics

Race	White	Black	Hispanic	Asian	Native American	Other	Total	p-values
Patients n(%)	26395(82.8%)	2155(6.7%)	1865(5.8%)	555(1.7%)	175(0.5%)	725(2.2%)	32785	<0.001
Age (mean in years)	68	63	63	66	64	65	67	<0.001
Age ≥18 to <49 years	6.5%	15.6%	16.9%	14.0%	8.6%	10.3%	9.8%	<0.001
Age ≥49 to <59 years	18.3%	21.1%	21.5%	15.0%	28.6%	22.1%	17.0%	<0.001
Age ≥59 to <69 years	25.8%	25.3%	25.2%	19.0%	28.6%	27.6%	24.0%	<0.001
Age ≥69 years	49.5%	38.0%	36.5%	50.4%	34.3%	40.0%	49.0%	<0.001
Gender								
Male	16.4%	24.0%	20.8%	25.1%	17.7%	21.5%	10.6%	<0.001
Female	83.6%	76.1%	79.2%	74.9%	82.3%	78.5%	89.4%	<0.001
Hospital Region								
Northeast	20.2%	18.8%	19.0%	19.8%	5.7%	36.5%	21.0%	<0.001
Midwest	25.5%	22.0%	5.6%	11.7%	28.6%	9.7%	24.4%	<0.001
South	32.2%	49.9%	31.9%	7.2%	17.1%	29.7%	33.5%	<0.001
West	22.2%	9.3%	43.4%	61.2%	48.6%	24.1%	21.0%	<0.001
Median Household Income by ZIP Code								
0 to 25th percentile (low income)	20.3%	51.0%	32.9%	15.5%	38.2%	19.7%	25.2%	<0.001
26th to 50th percentile (median)	27.5%	20.3%	26.9%	17.3%	23.5%	19.7%	26.4%	<0.001
51st to 75th percentile	28.1%	18.0%	25.3%	20.9%	14.7%	28.2%	25.8%	<0.001
76th to 100th percentile (high income)	24.0%	10.0%	14.8%	46.4%	23.5%	32.4%	22.4%	<0.001
Insurance Type								
Medicare	64.7%	54.2%	50.4%	48.6%	57.6%	45.7%	64.4%	<0.001
Medicaid	6.9%	18.1%	20.9%	11.9%	12.1%	14.3%	11.1%	<0.001
Private Insurance	25.8%	21.0%	23.7%	33.9%	24.2%	33.6%	21.5%	<0.001
Uninsured	2.6%	6.1%	5.0%	5.5%	6.1%	6.4%	2.8%	<0.001
Hospital Location								
Urban	94.0%	96.3%	98.7%	98.1%	86.7%	98.6%	93.7%	<0.001
Rural	6.0%	3.7%	1.3%	0.9%	14.3%	1.4%	6.3%	<0.001
Type of Institution								
Teaching	74.2%	80.5%	82.0%	78.4%	77.1%	86.2%	76.1%	<0.001
Non-Teaching	25.8%	19.5%	18.0%	21.6%	22.9%	13.8%	23.9%	<0.001
Hospital Bed Size								
Small	16.8%	16.0%	16.9%	16.2%	31.4%	15.2%	17.7%	<0.001
Medium	28.3%	28.5%	30.6%	27.0%	17.1%	37.2%	27.5%	<0.001
Large	54.9%	55.5%	52.6%	56.8%	51.4%	47.6%	54.8%	<0.001
Hospital Metrics								
Length of Stay (days)	3.5	4.5	3.3	3.8	5.1	3.5	3.5	<0.001
Total Charge (USD)	53042	65635	71443	79111	71234	71272	55569	<0.001

Comorbidities	White	Black	Hispanic	Asian	Native American	Other
Congestive Heart Failure	34%	36%	29%	36%	37%	32%
Mood Disorders	2.4%	4.9%	2.7%	1.8%	5.7%	4.1%
Smoker	45%	45%	28%	23%	29%	30%
Hyperlipidemia	52.3%	47.6%	49.0%	53.2%	34.2%	49.0%
Obesity	11.8%	14.1%	14.8%	5.9%	15.7%	9.6%
Hypertension	38.3%	40.8%	43.7%	38.7%	31.4%	37.9%
Diabetes Mellitus	19.0%	27.6%	32.7%	31.5%	31.4%	24.8%
Charleson Comorbidity Index:						
0	25.1%	20.7%	25.1%	26.3%	26.3%	31.8%
1	28.6%	26.9%	29.7%	27.8%	27.8%	25.0%
2	21.4%	20.5%	20.9%	14.3%	14.3%	23.9%
≥3	24.9%	31.8%	24.2%	31.6%	31.6%	19.3%

Outcomes	White	Black	Hispanic	Asian	Native American	Other
Pulmonary embolism	1.4%	2.5%	1.7%	0.6%	1.0%	3.7%
Mortality	1.6%	2.0%	0.5%	1.8%	2.9%	4.1%
Stroke	2.3%	4.9%	2.7%	1.8%	5.7%	4.1%
Ventricular Arrhythmias	4.6%	5.8%	4.3%	2.7%	8.5%	7.6%
Cardiogenic shock	6.3%	8.3%	8.8%	11.9%	8.6%	7.7%
Cardiac arrest	1.7%	3.9%	2.1%	3.6%	5.7%	3.5%
Diastolic Heart Failure	3.4%	5.3%	4.0%	0.8%	2.2%	1.7%

Multivariate Logistic Regression

Outcomes	White		Black		Hispanic		Asian		Native American indian		Other	
	OR[a] (95% CI)	*Pv*	*OR (95% CI)*	*Pv*	OR[a] (95% CI)	*Pv*	OR[a] (95% CI)	*Pv*	OR[a] (95% CI)	*P-value*	OR[a] (95% CI)	*Pv*
Pulmonary embolism	0.53(0.4-0.5)	<0.001	1.9(1.4-2.4)	<0.001	1.2	0.2	0.4	0.09	0.7	0.6	2.76(1.8-4.2)	<0.001
Mortality	0.67(0.6-0.8	<0.001	1.5(1.2-1.7)	<0.001	1.4(1.1-1.6)	<0.001	1.97(1.5-2.5)	<0.001	1.2	0.4	1.8(1.4-2.3)	<0.001
Stroke	0.4(0.3-0.7)	0.003	2.1(1.3-3.4)	0.003	1.1	0.7	0.7	0.7	2.4	0.2	1.7	0.2
Ventricular Arrhythmias	0.8(0.7-0.9)	0.04	1.2(1-1.3)	0.046	0.9	0.7	1	0.8	1.2	0.4	1.3(1-1.7)	0.04
Cardiogenic shock	0.7(0.6-0.8)	<0.001	1.35(1.2-1.5)	<0.001	1.46(1.2-1.7)	<0.001	2.(1.6-2.5)	<0.001	1.4	0.17	1.2	0.12
Diastolic Heart Failure	0.6(.41- 0.94)	0.026	1.6(1.06 - 2.42)	0.03	1.2(0.73 - 1.93)	0.49	0.2(0.03 - 1.57)	0.13	0.7(0.09 - 4.78)	0.68	0.5(0.16 - 1.57)	0.23
Cardiac arrest	0.43(0.2 - 0.7)	0.002	2.3(1.3-3.9)	0.002	1.2	0.56	2.1	0.7	3	0.2	2	0.18
	Multivariate Linear Regression											
Length of Stay	-1.1(-1.6 to -0.5)	<0.001	1.1(0.48-1.6)	<0.001	-0.03(-0.4-0.36)	0.9	0.43(1.8-4.2)	0.17	1.75(-0.0-3.5)	0.045	0.4.(0.6-0.7)	0.9
Total Charge	-14442(-23931-4954)	<0.001	12019(1785-22252)	<0.02	15431(5497-25364)	0.002	22858(3377-42339)	0.02	15629(11045-42303)	0.251	18950(1959-35939)	0.029

[a]OR =Odds Ratio. Pv= p-value