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# Involvement of HLA in Serum Beta-2 Microglobulin levels among Mumbai HIV-1 Patients

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**Abstract:** HLA allele involves along with B-2 microglobulin (B2M) and T cell receptor in host specific immune response. HLA alleles are known for its extensive polymorphism in order to accommodate the maximum of antigenic peptides. Serum beta-2 microglobulin has been reported to have a prognostic value for predicting disease progression in HIV patients. In this study, we evaluated the serum B2M levels and the HLA profile among the 124 HIV patients and 94 Normal healthy controls from Mumbai. The B2M levels were estimated by conventional ELISA technique while the HLA A and HLA B were done using PCR – SSOP molecular kits. Our results revealed that HIV patients showed increased B2M levels (88.70%) range (2.5ug/ml – 60ug/ml) compared the controls (42.55%). HLA A*11:01:01 (OR=3.25; P value 0.0015), HLA B*35:01:01 OR=3.57;P value 0.0002), HLA B*44:03:01 (OR=5.32; P value 0.0036), haplotypes HLA A*11:01:01- B*35:01:01 (OR=5.68; P value 2.47E-05), HLA A*33:03:01- B* 44:03:01 (OR=19.95; P value 0.0003) were significantly increased among the B2M increased HIV patients. While HLA A*03:01:01:01(OR=0.18; P value 0.0061) was significantly decreased among B2M increased HIV patients. Our results reveal that the production of serum B2M levels correlates with the HIV disease progression. Therefore it could be of a prognostic value in HIV infection.

**Keywords:** HIV patients; B2M, HLA, Mumbai.

## 1. Introduction

Beta-2 microglobulin (B2M) is a protein found on the surface of white blood cells. B2M is expressed in all nucleated cells of the body and a component of MHC-class-I molecule. Human B2M is a low molecular weight protein (MW 11600) consisting of a single polypeptide chain of 99 amino acids present in chromosome 15. It is identical to the small chain of the HLA-A, -B, and –C Major Histocompatibility complex antigens. Levels of native B2M have been used to assess renal function in kidney transplant recipients (1). It has been suggested that B2M can be used as a prognostic marker for HIV infection. B2M is eliminated via the kidneys, found at low levels in the serum (Less than or equal to 2.7ug/ml) and urine (less than 1ug 24 hours 0-160ug/ml) of normal individuals. B2M is also excreted in increased amounts in the urine of patients with upper urinary tract infections and connective-tissue diseases such as rheumatoid arthritis and Sjogren's syndrome. Serum B2M has prognostic value similar to lymphocyte profiles for predicting disease progression in HIV infected individuals. Serum B2M values among AIDS patients, Intravenous drug users, and Pediatric HIV patients has shown a profound increase in many studies from African and other countries. This study aims to evaluate immune-genetic response for beta-2 microglobulin levels among HIV-1 infected patients and controls.

## 2. Materials and Methods

A total of 124 HIV-1 infected patients and 94 age and sex matched controls were included after KEM

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ethical committee approval. HIV-1 infected patients were confirmed for the HIV infection by rapid, ELISA and western blot tests using commercial kits. The controls from the same ethnic background had no HIV infection. The B2M levels were done using ELISA. The molecular HLA A and HLA B typing were done from the genomic DNA extracted (2) using PCR-SSOP HLA typing reagents the HL alleles were assigned as per the kit protocol. The standard statistical analysis was done as described (3).

## 3. Results

Our study revealed increased levels of B2M (88.70%) range (2.5ug/ml-60ug/ml) compared to the controls (42.55%) (Fig. 1). The HLA distribution among the B2M increased patients revealed that HLA A*11:01:01, HLA B*35:01:01, HLA B*44:03:01, haplotypes A*11:01:01-B*35:01:01, HLA A*33:03:01-B*44:03:01 were significantly increased while HLA A*03:01:01:01 was significantly decreased (Table 1).

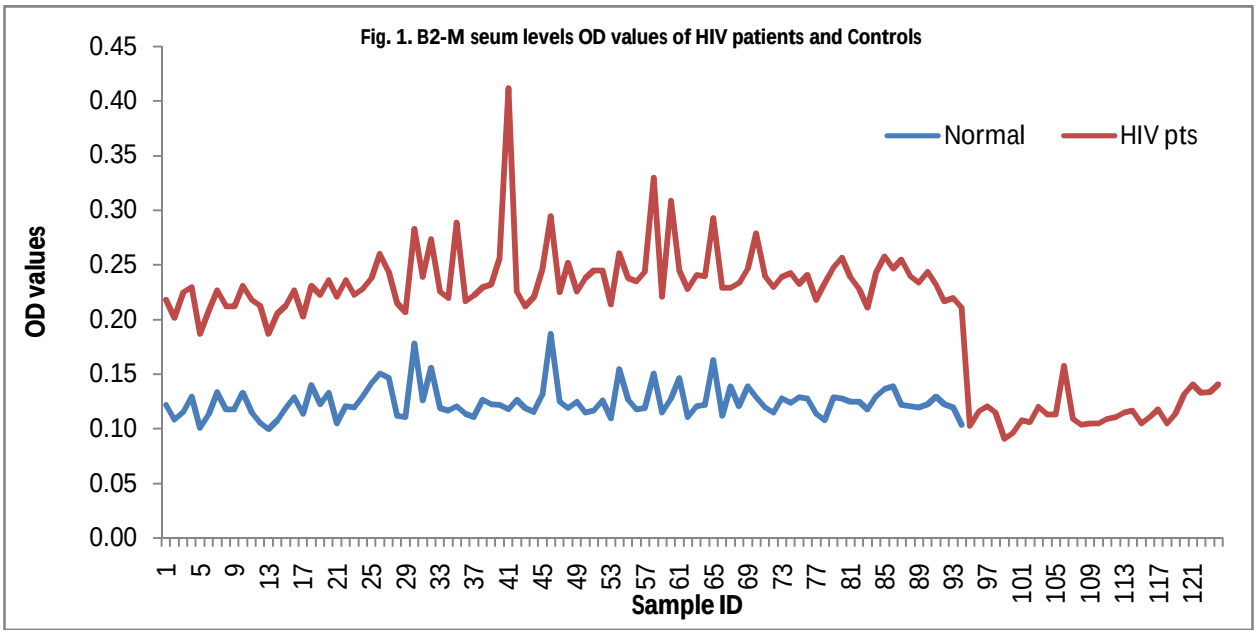


**Table 1. HLA distribution among B2M positive HIV-1 patients and controls from Mumbai.**

| HLA | Pts (N= 57) | Ctls (N=78) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | % AF | % AF | OR | Ki2 | EF | PF | 95% CI | P value | |
| **A*01:01:01** | 11.40 | 17.94 | 0.59 | 1.71 | | | 0.28-1.19 | | |
| **A*02:11** | 19.29 | 20.51 | 0.93 | 0.01 | | | 0.50-1.69 | | |
| **A*03:01:01:01** | **2.63** | **1.82** | **0.18** | **7.52** | | **0.08** | **0.05-0.63** | **0.0061** | ** |
| **A*11:01:01** | **22.80** | **8.33** | **3.25** | **10.03** | **0.15** | | **1.58-6.65** | **0.0015** | ** |
| **A*24:02:01:01** | 14.03 | 10.89 | 1.34 | 0.35 | 0.03 | | 0.64-2.71 | | |
| **A*26:01:01** | 7.01 | 1.28 | 5.81 | 4.57 | 0.05 | | 1.21-27.91 | 0.0325 | |
| **A*33:03:01** | 23.68 | 21.79 | 1.11 | 0.05 | 0.02 | | 0.62-1.98 | | |
| **A*68:01:01** | 2.63 | 3.21 | 0.82 | 0.08 | | | 0.19-3.48 | | |
| **B*07:02:01** | 13.15 | 14.74 | 0.88 | 0.04 | | | 0.43-1.76 | | |
| **B*08:01:01** | 7.01 | 1.28 | 5.81 | 4.57 | 0.05 | | 1.21-27.91 | 0.0325 | |
| **B*15:01:01** | 1.75 | 1.28 | 1.40 | 0.10 | | | 0.19-4.91 | | |
| **B*27:05:02** | 1.75 | 1.28 | 1.38 | 0.10 | | | 0.19-9.91 | | |
| **B*35:01:01** | **28.94** | **10.25** | **3.57** | **14.26** | **0.20** | | **1.84-6.87** | **0.0002** | ** |
| **B*40:06:01:01** | 21.92 | 17.30 | 1.34 | 0.63 | 0.05 | | 0.73-2.46 | | |
| **B*44:03:01** | **12.28** | **2.56** | **5.32** | **8.48** | **0.09** | | **1.70-16.63** | **0.0036** | ** |
| **B*54:01** | 3.50 | 1.92 | 1.86 | 0.18 | | | 0.40-8.46 | | |
| **B*57:01:01** | 12.28 | 16.66 | 0.70 | 0.69 | | | 0.34-1.41 | | |
| **Haplotypes** | **% HF** | **% HF** | **OR** | **Ki2** | **EF** | **PF** | **95% CI** | **P value** | |
| **A*01:01:01-B*57:01:01** | 11.40 | 16.02 | 0.67 | 0.81 | | | .32-1.38 | | |
| **A*02:11-B*40:06:01:01** | 17.54 | 14.74 | 1.23 | 0.21 | | | .63-2.39 | | |
| **A*11:01:01-B*35:01:01** | **21.05** | **4.48** | **5.68** | **16.19** | **0.17** | | **2.35-13.71** | **2.47E-05** | ** |
| **A*24:02:01:01-B*07:02:01** | 12.28 | 4.48 | 2.98 | 4.54 | 0.07 | | 1.16-7.64 | 0.033 | |
| **A*26:01:01-B*08:01:01** | 7.01 | 1.28 | 5.81 | 4.57 | 0.05 | | 1.21-27.91 | 0.032 | |
| **A*33:03:01-B*44:03:01** | **11.40** | **0.64** | **19.95** | **13.41** | **0.10** | | **2.56-154.95** | **0.0003** | ** |

N+ -Number Positive;OR - Odds Ratio; PF- preventive fraction **significant P value; %AF -allele frequency percentage;
Ki2 -Chi-square with Yates Correction;EF -etiological fraction;95% CI- 95% confidence Interval;%HF -Haplotype frequency percentage

## 4. Discussion

B2M is a protein component of MHC class I molecules, present in the surface of all nucleated cells, more in lymphocytes. B2M is a plasma protein produced by activated lymphocytes, levels increase in serum with HIV progressive infection in patients with AIDS Dementia complex, possibly another marker for HIV progression. Increased production or destruction of lymphocytes causes B2M levels to increase in blood. The B2M levels are increased among patients with progressive infection, like, multiple myeloma, connective tissue diseases Rheumatoid arthritis and Sjogren's syndrome (4), EA marker for long-term haemodialysed Chronic renal failure patients (5), amyloidosis (6), viral infected patients (7) and Lymphoproliferative disorders (8). The measurement of B2M levels in 369 STD patients, results revealed a prognostic value for HIV infection (9).

Earlier many results on HLA allele associations have been reported from India (10, 11 and 12). In the current study, we show that the haplotypes HLA A*11:01:01-B*35:01:01 and HLA A*33:03:01-B*44:03:01 associated increased with B2M serum levels from India.

## 5. Conclusions

Our study revealed that production of serum B2M levels correlates with the HIV progression. Therefore, it could be of prognostic value in HIV infection in developing countries.

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