



Prevalence of Discordant Immune Response in People with HIV1 Infection and Correlation Between Age, Gender and CD4 Levels.

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ABSTRACT:

Introduction: Discordant immune response (DIR) in patients with HIV1 infection on Antiretroviral Therapy (ART) results in high incidence of mortality. Additionally, little is known about the influence of age and gender on CD4 cell levels and the prevalence of DIR. Hence a study was undertaken to determine the prevalence of DIR in Indian HIV/AIDS outpatient department and study effect of age and gender on DIR in people with HIV-1 infection on ART to facilitate early intervention and implementation of better treatment strategies.

Objectives: To study the prevalence of Discordant Immune Response of patients with HIV 1 infection.

Methods: A retrospective chart review was undertaken to explore the prevalence of DIR, by reviewing the records of patients with HIV 1 infection visiting the ART clinic in a tertiary care hospital during the period of April 2021-April 2023. Demographic data (age, gender) and values of CD4, CD8 and Viral Load tests were entered in a password protected computer for analysis.

Results: Out of 1509 individuals who were tested for CD4 and Viral Load, 154 individuals were identified as immunologically discordant. The prevalence of immunological discordance to ART was 10.02%. Higher prevalence was seen in males and in people above 60 years. A weak negative correlation was observed between age and CD4 level in people with concordant immune response, however there was no significant correlation found in patients having discordant immune response.

Conclusions: Prevalence of DIR in patients with HIV1 infection was 10.2% in Navi Mumbai, Maharashtra. This study highlights the complexity of achieving full immune recovery in HIV patients and the need for targeted approaches beyond viral suppression.

1. Introduction

Antiretroviral Therapy (ART) in patients diagnosed with HIV infection substantially reduces the incidence

of acquired immunodeficiency syndrome (AIDS), with increase in CD4 cell count being significantly and independently associated with recovery. However, some patients do not achieve rise in CD4 cell count



following ART despite achieving viral suppression. This paradoxical response is known as immunological discordance. ⁽¹⁾

Studies report high prevalence of discordant immune response in people belonging to low-middle income countries. Global incidence for discordant immune response in studies from and Nigeria (22.6%), ⁽²⁾ Ethiopia (2.7%) ⁽³⁾, South Africa (24%) ⁽⁴⁾, Brazil (9%) ⁽⁵⁾ and Europe 12%, 15% ^(6,7) Only one study from western India, reported 9.7% prevalence of immune virological discordance. ⁽⁸⁾

Incidence of mortality is reportedly higher in participants with discordant immune response (DIR) compared to people without DIR. The most commonly reported pathologies associated with high mortality are tuberculosis, AIDS related cancers, *pneumocystis jirovecii* and bacterial pneumonia. ⁽⁹⁾

Discordant responses (DIR) are associated with an increased incidence of AIDS events such as cancers. Further, there is an associated risk of increased incidence of non-AIDS events such as stroke, liver failure, renal failure, endocarditis, meningitis, and all-cause death. ⁽¹⁰⁾ For the majority of included studies, mortality in patients with DIR was two to three times higher than in those with a satisfactory immune response ⁽¹¹⁾

As the frequency of discordant immune response in patients on ART varies greatly in care centres around the world, it is important to determine the prevalence of immunological discordance in Indian HIV/AIDS outpatient departments.

Additionally, little is known about the influence of age and gender on prevalence of discordant response. Thus, this study was designed to determine the prevalence of discordant immune response and effect of age and gender on discordant immune response in people with HIV-1 infection on ART to facilitate early intervention and implementation of better treatment strategies.

2. Methods

Following ethical approval, a retrospective chart review was undertaken to explore the prevalence of immunological discordance.

Data was obtained by reviewing the records of patients who were tested and registered at the ART Outpatient clinic at a tertiary care hospital in Navi Mumbai. Data was retrieved for a two-year period from April 2021 to April 2023.

Screening for prevalence of discordant immune response was done by reviewing the records which contained records of all patients tested for CD4, CD8 and Viral Load. These tests were performed at a NABL accredited lab at MGM Medical hospital, Navi Mumbai. All the data were entered in a password protected computer in an excel sheet classifying the information in terms of age, sex, Viral load CD4 and CD8 levels. The data was coded to maintain privacy and confidentiality of the patients.

3. Result

Out of the 1509 individuals tested for CD4 and Viral Load during this period, 154 were identified as immunologically discordant, resulting in a prevalence rate of 10.02% for immunological discordance to ART.

A closer examination revealed that the prevalence of discordant immune responses was higher among males (13.3%) compared to females (6.4%). With respect to age distribution, analysis of 1459 samples with information on age, our observations indicated that the highest prevalence of discordant immune responses was in individuals over 60 years old (16%).

This was followed by the age group of 41-60 years, which had a prevalence rate of 11.6%, and the age group of 21-40 years, with a prevalence of 9.2%.

A very weak negative correlation was observed between CD4 cell levels and age in concordant males (Pearson's correlation coefficient 0.131, $p < 0.001$) and females (Pearson's correlation coefficient 0.104, $p = 0.009$). However, there was no significant correlation found in patients having discordant immune response.

Gender	Total No. of patients	No. of discordant patients	% Prevalence
Male	822	110	13.3
Female	667	43	6.4



Transgender	20	1	5
Total	1509	154	10.2

Table.1 Classification of discordant immunological response on basis of gender.

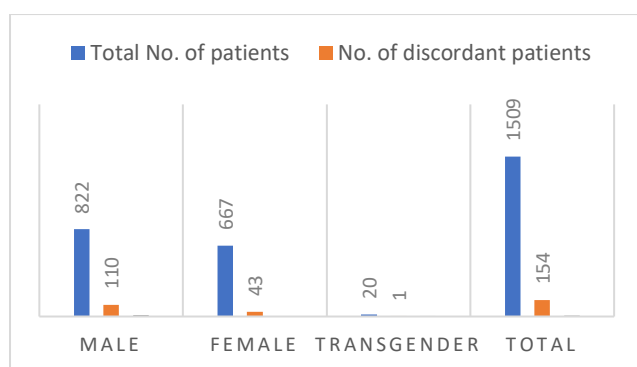


Fig.1 Number of individuals having discordant immune response on basis of gender

Age group	Total No. of patients (n=1459)	No. of discordant patients	% Prevalence
1-20 years	73	3	4.1
21-40 years	553	51	9.2
41-60 years	758	88	11.6
Above 60 years	75	12	16.0

Table 2. Classification of discordant immunological response on basis of age.

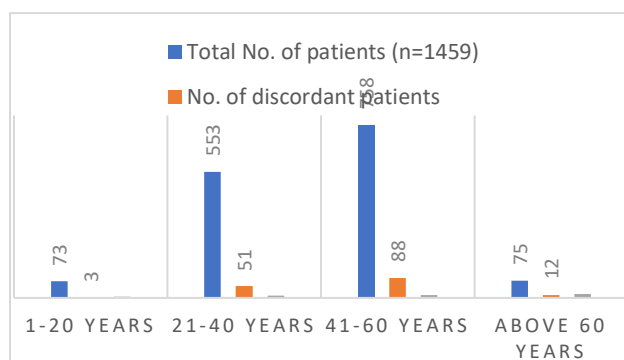


Fig.2 Prevalence of discordant immune response on basis of age.

4. Discussion

The prevalence of immunovirological discordance (DIR) in our study was 10.2%, which is quite similar to the study from Western India which reported it to be 9.7%⁽¹²⁾. DIR represents a significant challenge in the management of HIV, where patients achieve viral suppression but fail to experience proportional immune recovery. This discordance can be attributed to persistent inflammation, immune system exhaustion, and residual viral reservoirs. Chronic immune activation and inflammation continue to impair immune recovery, even when viral loads are suppressed, contributing to DIR. These findings underscore the complexity of achieving complete immune restoration beyond mere viral suppression.

Our study found a significantly higher prevalence of DIR in males compared to females. This finding is consistent with studies from Ethiopia⁽¹³⁾, Nigeria⁽¹⁴⁾ and Rwanda⁽¹⁵⁾, which also report a higher risk of immunological nonresponse in males. The higher prevalence in males may be related to lower baseline CD4+ counts and poorer health-seeking behavior and treatment adherence compared to females. Studies suggest that males generally have lower baseline CD4 counts, which can impact immune recovery⁽¹⁶⁾. Additionally, hormonal differences, such as lower testosterone levels in males, may contribute to reduced immune function and CD4+ T-cell counts. This aligns with findings from a multicentric study in India, which reported significantly higher absolute CD4+ T-cell counts in females. Male discordant individuals in our study had lower CD4 values compared to their female counterparts, supporting the notion that gender-related differences in immune response are significant.⁽¹⁷⁾

DIR prevalence was highest in the age group above 60 years (16%) which was followed by 41-60 years (11.6%). The negative correlation observed between CD4 cell levels and increasing age in patients with concordant immune responses is consistent with existing literature. Older age is a known risk factor for immunological discordance due to decreased thymic function, which impacts the ability to regenerate naïve T-cells and achieve complete immune restoration.⁽¹⁸⁾ However, in discordant individuals, there was no significant correlation between CD4 levels and age, suggesting that factors beyond age, such as comorbidities and treatment regimens, may also influence DIR.



5. Conclusion

Our study found a DIR prevalence of 10.2%, with highest discordance was found in males (13.3%) and in those over 60 years old (16%), with decreasing rates in younger age groups. DIR presents a challenge in HIV management, where despite viral suppression, immune recovery remains incomplete due to chronic inflammation, immune exhaustion, and residual viral reservoirs. These findings highlight the complexity of achieving full immune recovery in HIV patients and the need for targeted approaches beyond viral suppression. Hence, intensive adherence support, and counselling may be deemed essential in Indian health care setups.

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