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A Review on Various Aspects of HIV Infection

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Abstract

Many people are affected by HIV infection worldwide, lack of ability of modern medication in developing an active vaccine against HIV is a global public health importance. Various aspects such as diseases associated with HIV infection, role of immune cells in diagnosis and treatment, significance of molecular changes during infection, complications in infants, impact of gender and social behaviour and diagnosis of disorders associated with HIV infection were discussed in this review. Affected patients would be associated with acute kidney injury, arterial stiffness, cardiovascular disease, Tuberculosis, intestinal parasite carriage and disruptive sleep apnea. Immune cells like CD4, CD8, CD38 T cells and natural killer cells have a vital role in diagnosis and treatment. DNA vaccines could play a major role to prevent or treat infectious diseases including HIV and would elicit T cell immunity, protective antibody responses and local mucosal immunity protective vaccine against HIV infection. Health professionals are responsible for diagnosis of disorders associated with HIV infection and follow-up of HIV-infected paediatric patients. There is a crucial need to improve and evaluate novel interventions that are tailored for this helpless population. Several factors such as income deficit, Pre-college residence, pornographic film viewing and believe in sexual abstinence for HIV prevention were found to be significant predictors of initiating premarital sex. Younger generations could be advised to maintain the virginity as cultural norm. Incorporation of socio-structural elements and geospatial techniques in analytical approaches would lead to better understanding of local dynamics and develop mediations that increase our facility of targeted HIV prevention services.

Keywords: HIV infection; DNA vaccine; Immune cells; antiretroviral therapy; Prevention

Introduction

Clinically, HIV infection can appear in various forms. In general doctors would look for bodily signs that are associated with the disease. This is not defective because, statistics shows different presentations of HIV infection [1]. There is a link between nutrition, age and locomotors disorders in HIV infected persons, particularly who are above 45 years with body mass index ≥ 25 kg/m^2, are suggested to limit physical activities. Those people are less likely to have locomotors disorders. African societies face social and medical challenge in aged people living with HIV infection as they are dependent [2]. HIV-infected individuals could now enjoy a near normal life expectancy due to the many advances in the field of HIV medicine [3].

Numerous studies on the biology, pathophysiology or therapy of HIV-associated malignancies are single-center experiences with few randomized controlled trials. Hence, multi institutional collaboration is mandatory. AIDS Malignancy Consortium (AMC) is a clinical trials group supported by the National Cancer Institute, specifically focused on performing clinical and laboratory studies in HIV/AIDS patients with cancer [4]. Concern for HIV infected patients extend beyond medical and psychiatric complications. Many caregivers develop symptoms of depression and anxiety leading them to burnout and also there was high level of depression in HIV patients. Hence every HIV patients attending the clinic should also be assessed thoroughly for depression [5]. When there is no effective HIV vaccines, behavior change is the key to prevention efforts [6]. Social Health Insurance consultancy program delivered by nurse's support to increase HIV patients' willingness to obtain it [7].

HIV causes progressive weakening of the immune system in humans and after 30 years its role to the exhaustion of immune system is still understood only to some extent. Progression of AIDS was been predicted by generalized immune activation which is associated with HIV infection [8]. Comparative studies could help to identify co-factors responsible for aids. With clear idea about the cofactors related to disease, diagnosis and treatment of HIV infection can be improved and therefore AIDS could be prevented [9]. Reactive Oxygen Species (ROS) are essential molecules that control signal-transduction pathways and play main roles in immune defences, cell survival and death. Indicating protein-protein interaction between HIV proteins and elements involved in ROS production could reveal potential targets for therapeutic mediation [10].

Immunosuppression stimulated by HIV infection is different from other microbial infections and solely complicated to be unidirectional manipulation. To define HIV pathogenesis and immunity Explanation of the mechanistic events involved in virus replication joined with the incurred perturbations in the host innate and adaptive immune signalling pathways are of utmost important [11]. Joint appearances in HIV are usually seen. These manifestations must be satisfactorily addressed to improve the illness of a HIV patient. Proper and well-timed treatment will prevent development of abnormalities and improve quality of life [12]. Everyday HIV treatment remains an undeniable and arguably challenging barrier to adherence and, eventually viral suppression and epidemic control. These barriers should be targeted by identifying specific strategies [13].

Clinical benefits combined with a prominent effect on transmission risk by early initiation of ART provide important individual and population benefits over delayed ART. Though working attentions will require mobilization of additional resources, adherence to the new guidelines will confirm that the most effective therapy is available to fight and end the HIV epidemic [14]. For HIV-infected patients treated with multiple drug therapies, bariatric surgery is safe. Decrease in capsule burden as a direct concern of such procedure. Though,

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all candidates are not suitable to proceed to surgery, appropriate candidates should be picked by medical team in experienced bariatric centre [15]. Statins are anti-inflammatory and antiretroviral drugs which could consistently assess for a probable effect on HIV disease advancement and outcomes [16].

Huge proportions of students were involved in multiple sexual partners and unprotected sex. Several factors such as income deficit, Pre-college residence, pornographic film viewing and believe in sexual abstinence for HIV prevention were found to be significant predictors of initiating premarital sex. Younger generations could be advised to maintain the virginity as cultural norm and use of condom during sex before marriage is to be suggested [17]. Incorporation of socio-structural elements and geospatial techniques in analytical approaches would lead to better understanding of local dynamics and develop mediations that increase our facility of targeted HIV prevention services [18]. Assumed disgrace seems to play a large role in HIV revelation decision making and that mediation to reduce internalized HIV stigma may support in efforts to increase HIV disclosure and thus reduce secondary transmission of HIV [19].

It is vital that health care providers talk over patients and educate them on changing behaviours for value life. This may comprise alcohol and other substances termination and other health-related behaviours that raise their chances to contract HIV [20]. Automated medical record and can proficiently achieve link to medical and mental health care [21]. The theorized referral game could be explored by further studies to progress the care. [22]. It is possible to describe the burden of disease in aging patient groups under medical observation. Antiretrovirally treated patients had a greater burden of comorbidity and symptoms but not than HIV-negative patients with diabetes mellitus. Hence there is a need for prevention strategies with regard to neurologic, renal, cardiovascular and malignant diseases in this patient population [23]. Fist tournament is traditional practices in South Africa increase the risk of HIV infection due to lack of awareness. Government and scientific community could educate the people regarding the preventive measures [24]. Cytomegalovirus causes serious opportunistic infections with a high mortality rate. It requires a systematic suspicion among immune-compromised patients for early diagnosis and appropriate management in order to avoid delayed treatment linked to an unfavourable mortality [25].

Review of Literature

Diseases associated with HIV infection

HIV-infected patients would have Acute Kidney Injury (AKI), which is a usual complication which has been connected with prior renal impairment and are at increased risk during hospitalization, due to sepsis, volume reduction and acute administration of nephrotoxic medications or radio contrast. Even though highly active antiretroviral therapy has been long-term outcome of HIV-infected patients, mortality of HIV-infected patients with AKI is still high. Future research could be focused to elucidate pathophysiology and development of new therapeutic strategies for preventing AKI in HIV-infected patients [26]. Arterial stiffness is increased in both treated and non-treated HIV patients, chance of having cardiovascular disease increases in them. Factors such as aging, increased blood pressure and metabolic syndrome were stated to affect arterial stiffness. There should be improvement in diagnosis and management of cardiovascular risk factors among HIV positive patients. There is need for collaboration between clinicians and basic science researchers to bridge the gap in respect to lack of information on HIV and cardiovascular diseases [27].

Even though Cervicofacial Actinomycosis (CA) is not commonly observed in dentistry, proper diagnosis should be done to avoid further complications. When HIV infected patient diagnosed with CA, proper treatment could prevent destructive consequences [28]. There were unusual radiological features in pulmonary tuberculosis associated with HIV Infection. Furthermore, chest radiography is still recommended as a useful diagnostic test for pulmonary tuberculosis associated in HIV patients [29]. Occurrence of cardiovascular defects among the adult HIV patients attending Komfo Anokye teaching hospital was high. Major cardiovascular abnormalities observed were dilated cardiomyopathy, pulmonary hypertension and pericardial effusion [30].

Tuberculosis occurrence rates in the course of 2001-2004 persisted considerably lower when compared to 2005-2009. The period of the disease, its progressive stage with profound immunosuppression and late initiation of antiretroviral therapy are prognostic factors of tuberculosis in HIV-infected patients. Initial antiretroviral therapy and intensified tuberculosis screening are crucial to reduce incident tuberculosis [31].

When compared to HIV negative patients, incidence of Guillain-Barré Syndrome (GBS) is significantly increased in HIV-positive individuals. It could occur in any stage of HIV infection and is often the presenting indicator. Immune deregulation could be the cause for increased incidence of GBS in HIV-infected individuals and molecular mechanism of which permits further investigation [32]. HIV is more widespread in India which causes AIDS. Cancer diseases such as Kaposi sarcoma, non-Hodgkin lymphoma and cervical cancer are subsequent in HIV patients. Homosexual men are affected by Kaposi Sarcoma associated Herpes virus which is sexually transmitted [33].

When compared to HIV negative patients, there was no much difference in intestinal parasite carriage among HIV infected patients. Though, further studies are required to establish the national epidemiological profile of intestinal infection during HIV carriage in order to guide policy makers and medical staff [34]. The Intradural disc herniation is a very unusual pathology and could be suspected in few subsets of patients. Its diagnosis is preoperative and confirmed intra-operative through novel neuroradiology imaging [35]. HIV infected patients suffer from occurrence of night oxygen desaturation and disruptive sleep apnea [36].

Role of immune cells in diagnosis and treatment

Even though there are reports that reveal CD4+ and CD8+ T-cells were generated from progenitor cells with the help of OP9-DL1. It was been demonstrated for the first time that OP9-DL1 cells are capable to support the response and function of a diverse population of mature human thymocytes and also provide the required signals for *in vitro* infection with HIV. It was being clearly stated that co-culture of human thymocytes with OP9-DL1 cells result in greater IL-7 response when compared to co-cultures with thymic epithelial cells. This reveals that they are an appropriate candidate for exogenous stimuli on thymocyte function [37].

Anti-retroviral therapy administration would be substantial in management of HIV. Specific biomarkers need to be identified for sustained suppression and development of drug resistance. Improvement of general health may help to decrease HIV transmission rates. CD 38 quantification act as an alternative source and cost effective test that could serve as additional tool in management of HIV infected patients [38]. Multiple HIV proteins enhance CXCL10 production along with other inflammatory cytokines will increase localized Th1 cell leads to establishment, persistent infection and enhanced inflammation. Targeting CXCL10-CXCR3 pathway may serve as

powerful approach to suppress inflammatory signaling cascades and ensuing HIV-1 associated neuropathogenesis as well as inflammation induced tissue damage in periphery [39].

Eosinophils exhibit altered functions based on different phases of HIV infection. It was protective during asymptomatic phase and harmful during AIDS phase. When compared to HIV infected person, survival period of patients co-infected by human T lymphotropic virus-1 is longer. Eosinophils in elaborating cytokines either one of type Th1 or Th2, participate in general control of the T cells response. Hence, they could modify the evolution of HIV infection, especially in the asymptomatic stage [40].

Finding a cure for HIV has come to be one of the major worldwide challenges of the 21st century. Because of the endurance of naive CD4+ T cells and their capability to proliferate and differentiate upon antigen exposure into any of the memory cell subsets and effector CD4+ T cells, they definitely pose a main barrier to eradicate latent reservoir. There are numerous aspects that are to be addressed. Are molecular mechanisms responsible for latency of HIV is same in both naive and memory CD4+ T cells? Are histone deacetylase inhibitors vorinostat, panobinostat and romidepsin which are latency reversing agents effective in naïve CD4+ T cells? The author has concluded that suitable primary cell models of HIV latency in naive CD4+ T cells have to be developed. In addition, a better focus on the latent reservoir in naive CD4+ T cells is justified in any clinical intervention aimed at reducing the size of latent reservoir [41]. C-C Chemokine Receptor 5 (CCR5) is a key factor of HIV pathogenesis and disease progression, polymorphism and continual evolution of HIV Env glycoprotein which binds CCR5 as a coreceptor suggest that the interaction is critical to understand HIV biology. When the complex relationship between host and viral determinants of CCR5 usage in HIV infections is understood, it would lead to predict disease progress and create new approaches for therapeutic intervention [42].

HIV replication can inhibited through direct or indirect cytolytic and noncytolytic pathways by immune cells like NK, γδ T cells and NKT cells. Innate are potent cytotoxic effectors. These antiviral innate effector cells are exhausted or dysregulated in HIV-infected individuals with chronic disease, but could partially recover after successful antiretroviral therapy. Development of therapeutic strategies, combining innate cell stimulating compounds and antiretroviral drugs would optimally stimulate immunity [43]. Viral effect assays from resting T-cells allow us to predict the size of such reservoirs and the viral ability of the emerging strains. Most clinical samples are difficult to perform viral outgrowth assays. Exclusion of HIV from the central nervous system will remain as an important obstacle for the success of future therapies trying to cure HIV infection [44]. Glucocorticoids and their receptors play an essential role in the regulation of immune, endocrine, inflammatory and metabolic responses to a variety of challenges including pathogens exposure inflammation and stress. They are the basis of an adaptive program for short lived inflammatory response, but if inflammation continues, adaptive equilibrium between cortisol and its receptors limit metabolic and vascular complications [45].

Significance of molecular changes during infection

In spite of the progress made in the implementation of polymerase chain reaction in Togo, access to Early Infant Diagnosis (EID) of HIV remains to be reviewed. Implementation and accessibility seems to be difficult, role of government sector and proper administrative and technical procedures would help in early diagnosis in infants. This would help in management of HIV infected and children and thus reduce mortality [46]. Nucleic acid amplification testing technologies after running a third generation assay could be a recommended as highly sensitive and low cost algorithm for blood donor screening in low and middle income countries. The advantage of third generation assay is to ignore all antibody negative donors, which will save cost. However, very few validations were done in Sub Saharan Africa, where electricity, water and road access was a challenge [47].

In order to interpret variation in levels of oxidative stress biomarkers, antioxidant enzyme activities along with Glutothione S-Transferase is compared in relation to GSTM1 genotype. Moreover, genotyping techniques with the capability to distinguish between individuals carrying one or two copies of the GSTM1 gene leads to thorough analysis of the polymorphism effects. This would be used as clinical marker to quantify risk for oxidative damage in HIV-infected patients [48]. Secreted Single Chain Variable Fragment (sscFv) Targeting CCR5 can protect gene-modified HIV target cells and it has potential to prevent unmodified target cells infection. Further, more potent sscFv targeting surface CCR5 may be designed to confer protection to target cells which are unmodified [49].

DNA vaccines could play a major role to prevent or treat infectious diseases including HIV and would elicit T cell immunity, protective antibody responses and local mucosal immunity protective vaccine against HIV infection. In animal models and humans, humoral and cellular immune responses are induced by DNA vaccines. They are effective particularly as a key component of HIV vaccination strategies, usually as part of a prime/boost vaccination strategy with viral vector evaluated for both preclinical studies and in Phase I and II clinical trials. Generation of vaccine-specific multifunctional CD8+ T cells would be a major component of an effective vaccine [50].

Complications in infants

Health professionals are responsible for diagnosis of disorders associated with HIV infection and follow-up of HIV-infected pediatric patients, it is critical to achieve early detection and subsequently being capable of improving the quality of life of both patients and their families [51]. Occurrence of HIV in children is high in the Eastern India, maximum was observed as maternal to child transmission. [52]. HIV positive children should have a monotonous neuropsychological assessment at intervals as part of their standard care to detect children with cognitive impairment on time [53].

The World Health Organization has framed inclusive methods to prevent HIV infection in infants and young children. HIV transmission to infants and young children could be prevented by avoiding infection in women; prevention of unplanned pregnancies among HIV infected women, providing care and support. Specific mediation to reduce mother to infant HIV transmission which include antiretroviral drug use, safer delivery practices and infant-feeding counselling and support [54]. To focus on paediatric HIV infection, few guidelines for use of antiretroviral agents were established by the HHS panel on antiretroviral therapy and medical management of children living with HIV, which is a working group of the office of AIDS research advisory council [55]. Birth testing could require slight programmatic effect on the proportion of children who initiate timely ART and survive, unless it is united with progresses in the cascade of care and further health system establishment. Focus should be more on decreasing the turnaround time and retention in care [56].

A combined effort is required to prevent HIV infections among children, it should be ensured that the mothers stay healthy and improve the diagnosis and treatment of HIV for children [57]. Clinical trials are likely preventable by early instigation of ART to improve immune status, there is a need to promote an earlier access to ART in

HIV-infected children [58]. Clinical measures are likely preventable by primary initiation of ART to increase immune status, there was a need to promote an earlier access to ART in HIV-infected children [59].

Impact of gender and social behaviour

There were differences in epidemiological and clinical characteristics among Mexican women that could have had an impact on their virological and immunological responses. Improving women's adherence to HIV treatment in Mexico would need eliminating obstacles to the national health care system and widespread health care services and implementing programs that take into account women's role as maternal caregivers. The author highlights the need to integrate social elements of health associated with gender inequality and social position when analysing treatment response [60].

Even though significant progress has been made in recent times to fight against HIV/AIDS, several key affected populations continue to struggle with high rates of HIV infection and lack of knowledge on HIV prevention and treatment programs. Transgender women are one such group, affected with high rates of HIV infection and extreme discrimination and violence. There is a crucial need to improve and evaluate novel interventions that are tailored for this helpless population. Structural intervention should be made in law and policy [61]. Large number of HIV positive men and women wished to have children and reproductive choices of HIV patients are not only affected by their HIV status but be subject to different predictor factors [62].

There were high occurrence rates for Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), Injection Drug Users (IDUs) and RuJu in Taiwan. These findings suggestively prove vulnerability and high-risk IDUs. Use of condom was very less among male IDUs and RuJu (the practice of inserting beads beneath the skin of penis). It was suggested that RuJu should be comprised in measures of sexual risk and addressed in HIV prevention [63]. Huge numbers of couples who live together are HIV discordant. The HIV negative partners in such setup are open to HIV infections. When those couples try to satisfy their sexual need and achieve preferred pregnancy would lead to sexual risk behaviour. There should be proper treatment options for the inconsistent couples to meet their needs at reduced rate of infecting the negative partner [64]. HIV risk of Thai army conscripts which denote Thai young men. There were number of risk factors from univariate analysis which include heroin, drug use before sex, perception of HIV risk and no fear about HIV [65].

Even if homosexuals have certain knowledge about HIV response, they have deprived awareness of safer sex and behaviour change [66]. Mediation that addresses one or two psychosocial health problems may synergistically decrease chances of HIV seropositivity among these needy Tanzanian homosexuals [67]. There was maximum detection rate of HIV among homosexuals who donate blood. They should be restricted to participate in blood donation to prevent infection and also to reduce the volume of blood processing and wastage [68]. Practice of anal sex mainly among younger men occurs in Tanzania. It should be conferred that thorough understanding of social, behavioural and environmental factors to be targeted in prevention programs [69]. HIV infection in men with similar clinical characteristics is not significantly associated to ambulatory function. Further studies are required to investigate HIV-infected adults with age-related factors that predict mobility and mortality [70].

Recent studies on HIV infection

A research initiative by amfAR's Countdown to a Cure for AIDS has targeted to develop the scientific basis for a cure by 2020. Which was been launched in February 2014, the Countdown is planned to intensify amfAR's cure-focused HIV research program through strategic investments of $100 million over the next five years. Few recent research findings are mentioned in this review. When compared to NK cells neutrophils are six times better to kill HIV-infected cells when antibodies were present. Neutrophil-mediated effector responses could be investigated in future HIV vaccine trials [71]. Transmission of HIV by dendritic cells might have essential implications for viral persistence *in vivo* in environments where residual replication could persist in the face of antiretroviral therapy [72]. Treatment with immune check point inhibitors might have dual benefits in HIV infection in acting on the cancers frequently associated and also by helping to purge the HIV reservoirs that indefinitely persist despite antiretroviral therapy [73]. The role of ruxolitinib in decreasing inflammation associated with HIV infection is being evaluated in a National Institutes of Health-funded clinical trial. Inflammation is alleged to contribute to the persistent HIV reservoir, the primary barrier to a cure [74].

Continuous improvement in access to HIV diagnosis and treatment rests at the core of the global response headed for attaining the target of ending AIDS as a public health threat and providing universal health coverage. On the other hand, HIV infection remains a foremost cause of illness and death in many countries, particularly in sub-Saharan Africa. Evidence till date suggests that reacting to advanced HIV disease would continue to be main public health priority for several years in future. WHO encouraged National HIV programs to implement the package of interventions and WHO update this package according to new evidence and implementation experience.

Conclusion

HIV vaccine exploration over the last two decades has been a tale of early courage, worldwide conversation now is more concerned with how to progress scientific research to develop at least partially defensive vaccine becomes a possibility. On the other hand, Education seems to be utmost in effect to decrease transmission of infection. There is need for teamwork between clinicians and basic science researchers to bridge the gap in respect to lack of information on HIV. Role of government sector and proper administrative and technical procedures are much more important in this aspect. Collaborative research on diseases associated with HIV infection, role of immune cells in diagnosis and treatment, significance of molecular changes during infection, complications in infants, impact of gender and social behaviour and diagnosis of disorders associated with HIV infection might help in HIV-infected individuals could now enjoy a near normal life.

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