

INNATE IMMUNITY AGAINST HIV AMONG HIGHLY EXPOSED SERO- NEGATIVE (HESN) FEMALE SEX WORKERS

1.0 RATIONALE FOR THIS SYSTEMATIC REVIEW

1.1 BACKGROUND

In 2010, the UNAIDS (Joint United Nations Program on HIV and AIDS) evaluates that the greater part surprisingly living with HIV/AIDS are women. It is assessed that, in Africa, ladies are twice as liable to contract HIV-1 through sexual intercourse involving vagina contrasted to men and are along these lines thought to be vulnerable persons in the population. The improvement of a female microbicide that gives security against HIV-1 infection is a promising preventive and precaution strategy.

Lajoie J et al revealed in a study in 2012 that throughout the years, numerous variables have been related with both powerlessness to, and insurance from, HIV-1 acquisition, yet probably the most intriguing discoveries have risen up out of the depiction of HIV-highly exposed seronegative (HESN) individuals.

Lajoie J et al further stated that despite rehashed presentation to the virus through life style, these people demonstrate a characteristic protection from HIV-1 and have been distinguished in different cohort over the world. The investigation of these partners has prompted the identification of various elements connected with security from HIV-1 procurement. Many examinations have inspected the immunological and hereditary connects of assurance among these ladies and have shown the nearness of foundational HIV-particular T-cell responses, polymorphisms in the IRF1 (interferon regulatory factor 1) quality, and expanded mucosal levels of antiproteases.

Elijah M. et al in 2012 revealed that among all disease, HIV/AIDS is among the highest ranks with regards to the disease that perpetuate devastating scourges to humans. From the insurgence of the disease in 1983, well over 30 million persons have demised from the disease and yet another about 33 million persons are living with the virus currently. Sub-Saharan Africa is known to be the region with the largest burden with some countries reporting as high as 40% among women who present for ante-natal clinic visits.

The study also stated that, although there are numerous developments done and currently ongoing with regards to antiretroviral therapy, there is still a high level of under coverage and in addition, the rate of incidence of new infections far outweighs those on therapy and thus vaccination, like in other viral control and prevention appears to be the best approach.

The study made it clear that, the main factors militating against the development of an efficacious and effective vaccine is the integrating nature of HIV virus into the genome of the host as well as its property of routinely mutating and thus blocks components of immune system that elicit production of antibodies that are protective.

The occurrence of people that are very exposed to the virus but seem not to acquire the infection gives assurance for a more concrete knowledge of correlates for protection that may result in an efficacious vaccine. Highly exposed seronegative (HESN) persons have been recognized among female sex workers. This finding caused a shifting of the initial focus on the apparently effective protection of CCR5 Δ 32 allele in HIV-1 infection to host genetics as the possible cause of infection resistance to the virus.

The study was conducted in order to identify genetic makers and biomarkers that are specific to highly exposed seronegative persons. This was achieved through a global whole blood

gene expression profiling of highly exposed HIV-1 , uninfected persons among well known female sex worker in Nairobi of Kenya.

1.2 IMMUNOLOGY OF THE FEMALE GENITAL (FGT)

The immunology of the genital tract of females is subdivided into 3 noteworthy territories showing particular phenotypic profiles: the vagina which is nonsterile and ectocervix colonized by microbes in commensalism to the host, the endometrium which is sterile and fallopian tubes, and the endocervix in which sterility might be transiently identified with menstrual cycle stage. In this way, female genital tract immunity is firmly directed by a hormonal as well as inflammatory processes all through the menstrual cycle, dealing with the weight of reproduction and microbial control. The intrinsic resistant compartment of the female genital tract includes the mucous coating of a tight epithelial cell obstruction, stratified at the vaginal and ectocervical levels, and dendritic cells , Langerhans cells , macrophages, natural killer cells, and neutrophils, which present assurance through the generation of antimicrobial agents, chemokines, and cytokines . Control of microflora and attacking pathogens is adjusted through pattern recognition receptors (PRRs, for example, toll-like receptors and NOD-like receptors, which perceive particular basic microbial/pathogen-related molecular patterns. In that capacity, genital epithelial cells frame a continuous obstruction between the lumen and basal cells and express pattern recognition receptors, e.g. , toll-like receptor-1 to - 9, demonstrating the possibility to react to an extensive variety of organisms/pathogens . Dendritic cells additionally express a vast range of pattern recognition receptors, and the communication amongst Epithelial cells and

submucosal Dendritic cells likely adjusts the upkeep of homeostatic harmony amongst resilience and irritation in the female genital tract.

1.3 AIMS AND OBJECTIVES

This review aims to look into the natural protective mechanism in the female genital tract in order to critically evaluate current evidence to determine the innate immune protection against HIV/AIDS virus among highly exposed seronegative commercial female sex workers.

2.0 RESEARCH

2.1. ELIGIBILITY CRITERIA

2.1.1. Inclusion Criteria

Participants – Studies involving female commercial sex workers will be included in this review. Also seronegative noncommercial sex worker female who are not highly exposed to HIV virus.

Interventions – Interventions involving the use of biomarker assays of female genital tracts from different sexually active female groups. Intervention for comparison will include the number of sexual intercourse years as well as the number of sexual partners.

Outcome – The primary outcome of interest is the incidence of HIV/AIDS acquisition assessed by HIV test with plasma. The secondary outcome of interest are the levels of viral load in those already affected in relation to the immune biomarker levels in the female genital tract.

2.1.2. Exclusion Criteria

Participants – Studies involving only non-high-risk seronegative females will be excluded from this review. Studies talking generally about HIV prevalence will be excluded. Also studies relating only other sexually transmitted disease alone will not be included in this review.

Interventions – Studies that include just prevalence of HIV/AIDS among female sex workers without any relation to HIV/AIDS acquisition level will be excluded from this review

Outcome – Studies will be excluded if they do not have the primary outcome of interest in this review as one of their outcome and mortality.

2.4 RESEARCH QUESTIONS

- Is there a protective biological mechanism against HIV virus in female sex workers?
- What is the level of significance of this mechanism if present?

3.0 MAIN FINDINGS

Defenselessness to HIV disease is multifactorial however is extraordinarily improved by previous safe actuation. The mucosal condition of the female genital tract has a vital impact on the vulnerability and foundation of HIV contamination amid unprotected intercourse. Sexual exercises have been already connected with mucosal safe enactment, and this actuation is accepted to be an imperative factor in vulnerability to HIV. Here, we announced an alternate level of mucosal insusceptible initiation between ladies of the all inclusive community and those occupied with business sex work. All the more curiously, these distinctions show up inside the first

principal year of inception to business sex work and turn out to be more articulated as the length of sex work increments.

High-risk people build up a more grounded intrinsic innate resistant reaction signaling natural effectors toward the genital compartment. Higher extent of actuated Natural Killer cells with more cytotoxic limit have been seen in the blood of highly exposed people and connected with insurance against HIV infection. Therefore, nonstop introduction to sex antigens through sex work may support the advancement and enlistment of a more grounded natural reaction to the female genital tract and add to HIV security. A diminished level of dendritic cells in the female commercial sex workers contrasted with the generally safe ladies. The number of dendritic cells at the female genital tract of commercial sex workers indicated less insusceptible initiation. In addition some of the reviewed studies also showed that cervical mononuclear cells from female sex workers had a higher extent of CD4+ T cells yet a lower extent of that subset signaled the HIV co-receptor CCR5.

In female commercial sex workers, the mucosal invulnerable initiation appeared to support the actuation of the natural framework without expanding the quantity of potential target cells.

Without a doubt, sexually dynamic non-commercial sex worker had higher mucosal levels of proinflammatory cytokines/chemokines and a higher extent of vaginal CD4+ CCR5+ T cells, CD8+ T cells, and CD8+ CCR5+ or CD8+ CD69+. Moreover, when contrasting the angle example of the cytokine/chemokine articulation between the foundational and the mucosal condition, we watched the distinctive example. In fact, in FSWs the levels of MIG, MIP-1a, and MIP-1b were essentially higher in the fundamental versus the mucosal compartment. These 3

chemokines are vital for the trafficking of activated T cell, which recommends that in FSWs there isn't solid enlistment of activated CD4⁺ T cells to the female genital tract. In any case, this nonappearance of contrast in the okay ladies could likewise be because of the little example size of this gathering. An investigation of sex specialists from Benin contrasting HIV-negative FSWs with HIV-positive commercial sex workers demonstrated a comparative finding. To be sure, there was less MIP-1a, MIG, and MCP-3 in the genital tract of females of HIV-uninfected commercial sex workers, and the slope of articulation in this gathering was not quite the same as the one saw in HIV-positive FSWs

Other findings from the reviews include; sensational changes in mucosal safe framework appear to show up as right on time as multi year after commencement of sex work. These outcomes are somewhat astonishing, in that the early commercial sex workers members showed diminished, not expanded, levels of invulnerable initiation. Discharge is known to contain proteins as well as CD4⁺ T cells, macrophages, and epithelial cells that express customer determined HLA-antigens and sans cell HLA antigens. In HIV contamination, the viral coat additionally contains HLA proteins. Diminishes et al demonstrated that the accomplice's HLA antigens in fundamental liquid could incite solid mucosal allo-invulnerable reactions in ladies amid unprotected sex, however at times rehashed vaccination to allo-antigens may prompt resilience. Our outcomes appear to validate this finding, demonstrating that rehashed presentation to various semen and antigens may prompt a specific resistance as showed by the lower cytokine/chemokine levels saw in those right off the bat in their sex work understanding.

This review was able to reveal that there is a dynamic decrease in mucosal safe actuation as span of sex work increments. That is, commercial sex workers who normally had a lower basal

invulnerable initiation and who react to allo-incitement with a more grounded down-direction of insusceptible actuation would be less inclined to end up HIV-tainted contrasted with ladies with fiery safe reactions in the primary long periods of association in sex work. After some time, this choice weight would enhance the HIV-negative FSWs pool for ladies with the immune quiescence phenotype, with a more grounded predisposition as length of sex work expanded. This bi-directionality is upheld by the way that when looking at the foundational invulnerable initiation between generally safe ladies and commercial sex workers , noteworthy contrasts were watched just between the okay ladies and experienced commercial sex workers (information not appeared), which appears to show that the IQ phenotype related with highly exposed seronegative ladies in this companion isn't just because of sex work.

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