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AWARENESS OF ANTI RETROVIRAL DRUGS IN HIV AMONG DENTAL STUDENTS

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ABSTRACT:
INTRODUCTION:The human immunodeficiency virus (HIV) is grouped to the genus Lentivirus within the family of Retroviridae, subfamily Orthoretrovirinae .On the basis of genetic characteristics and differences in the viral antigens, HIV is classified into the types 1 and 2 (HIV-1, HIV-2) . Before 1996, few antiretroviral treatment options for HIV-1 infection existed. The clinical management of HIV-1 largely consisted of prophylaxis against common opportunistic pathogens and managing AIDS-related illnesses.
AIM : To assess the knowledge and awareness of antiretroviral drugs in HIV patients among dental students.
MATERIALS AND METHODS: A cross sectional questionnaire was designed and distributed to 100 dental students. Questionnaire includes email address, questions aboutART, objectives of ART, group of antiretroviral drugs and newer drug for treating HIV infection. Data was collected, statistically analysed and results were obtained.
RESULTS: Among the study population, majority (90%) aware of antiretroviral therapy (ART) whereas 9% of the study population not sure about antiretroviral therapy and 1% of the study population not aware of antiretroviral therapy.
CONCLUSION: The findings observed in our study showed that awareness and knowledge of antiretroviral drugs for HIV patients among dental students were high. But, dental students were not aware of recent drug approved for adult patient living with HIV who tried multiple medications and whose HIV infection cannot be successfully treated.

KEYWORDS: Human immunodeficiency virus, Antiretroviral therapy, Zidovudine, Non – Nucleoside reverse transcriptase inhibitors, Nucleoside reverse transcriptase inhibitors, protease inhibitors.

1. INTRODUCTION:

The human immunodeficiency virus (HIV) is grouped to the genus Lentivirus within the family of Retroviridae, subfamily Orthoretrovirinae .On the basis of genetic characteristics and differences in the viral antigens, HIV is classified into the types 1 and 2 (HIV-1, HIV-2) (1). Before 1996, few antiretroviral treatment options for HIV-1 infection existed. The clinical management of HIV-1 largely consisted of prophylaxis against common opportunistic pathogens and managing AIDS-related illnesses. The treatment of HIV-1 infection was revolutionized in the mid-1990s by the development of inhibitors of the reverse transcriptase and protease, two of three essential enzymes of HIV-1, and the introduction of drug regimens that combined these agents to enhance the overall efficacy and durability of

therapy. Since the first HIV-1 specific antiviral drugs were given as monotherapy in the early 1990s, the standard of HIV-1 care evolved to include the administration of a cocktail or combination of antiretroviral agents (ARVs). The advent of combination therapy, also known as HAART, for the treatment of HIV-1 infection was seminal in reducing the morbidity and mortality associated with HIV-1 infection and AIDS (2-4). Combination antiretroviral therapy dramatically suppresses viral replication and reduces the plasma HIV-1 viral load to below the limits of detection of themost sensitive clinical assays (,50RNAcopies/ mL) resulting in a significant reconstitution of the immune system as measured by an increase in circulating CD4þ T-lymphocytes. Importantly, combination therapy using three antiretroviral agents directed against at least two distinct molecular targets is the underlying basis for forestalling the evolution drug resistance (5-7).

NRTIs were the first class of drugs to be approved by the FDA(8). NRTIs are administered as prodrugs, which require host cell entry and phosphorylation by cellular kinases before enacting an antiviral effect (9-11). Lack of a 30-hydroxyl group at the sugar (20-deoxyribosyl) moiety of the NRTIs prevents the formation of a 30-50-phosphodiester bond between the NRTIsandincoming50-nucleoside triphosphates, resulting in termination of the growing viral DNA chain. Chain termination can occur during RNA-dependentDNAorDNA-dependent DNA synthesis, inhibiting production of either the (2)or(þ)strands of the HIV-1 proviral DNA (12,13). Currently, there are eight FDA-approved NRTIs: abacavir (ABC, Ziagen), didanosine (ddI, Videx), emtricitabine (FTC, Emtriva), lamivudine (3TC, Epivir), stavudine (d4T, Zerit), zalcitabine (ddC, Hivid), zidovudine (AZT, Retrovir), and Tenofovirdisoprovilfumarate (TDF, Viread), a nucleotide RT inhibitor. As with all antiretroviral therapies, treatment with any of these agents often results in the emergence of HIV-1 strains with reduced drug susceptibility.[35-39]Resistance to NRTIs is mediated by two mechanisms: ATP-dependent pyrophosphorolysis, which is the removal of NRTIs from the 30 end of the nascent chain, and reversal of chain termination (14-16) and increased discrimination between the native deoxyribonucleotide substrate and the inhibitor.

NNRTIs inhibit HIV-1 RT by binding and inducing the formation of a hydrophobic pocket proximal to, but not overlapping the active site. The binding of NNRTIs changes the spatial conformation of the substrate-binding site and reduces polymerase activity (17,18). The NNRTI-binding pocket only exists in the presence of NNRTIs (19) and consists of hydrophobic residues (Y181,Y188,F227,W229,andY232),andhydrophilic residues such as K101, K103, S105, D192, and E224 of the p66 subunit and E138 of the p51 subunit. Unlike NRTIs, these non/uncompetitive inhibitors do not inhibit the RTof other lentiviruses such as HIV-2 and simian immunodeficiency virus (SIV). Currently, there are four approved NNRTIs: etravirine, delavirdine, efavirenz, and nevirapine (20).

The HIV-1 protease is the enzyme responsible for the cleavage of the viral gag and gag-pol polyprotein precursors during virion maturation (21). Ten PIs are currently approved: amprenavir (APV, Agenerase), atazanavir (ATZ, Reyataz), darunavir (TMC114, Prezista), fosamprenavir (Lexiva), indinavir (IDV, Crixivan), lopinavir (LPV), nelfinavir (NFV, Viracept), ritonavir (RTV, Norvir), saquinavir (SQV, Fortovase/ Invirase), andtipranavir (TPV,Aptivus). Because of its vital role in the life cycle of HIV-1 and relatively small size (11 kDa), it was initially expected that resistance to protease inhibitors would be rare. However, the protease gene has great plasticity, with polymorphisms observed in 49 of the 99 codons, and more than 20 substitutions known to be associated with resistance. The emergence of protease inhibitor resistance likely requires the stepwise accumulation of primary and compensatory mutations and each PI usually selects for certain signature primary mutations and a characteristic pattern of compensatory mutations. Unlike NNRTIs, primary drug-resistant substitutions are rarely observed in the viral populations in protease

inhibitor-naı¨ve individuals (22,23). Aim of the study is to assess the knowledge and awareness of antiretroviral drugs in HIV patients among dental students.

2. MATERIALS AND METHODS:

The study was conducted during the academic year december 2020 among the dental students.

STUDY SAMPLE SIZE:

The descriptive cross sectional study was based among 100 dental students .

INCLUSION AND EXCLUSION CRITERIA:

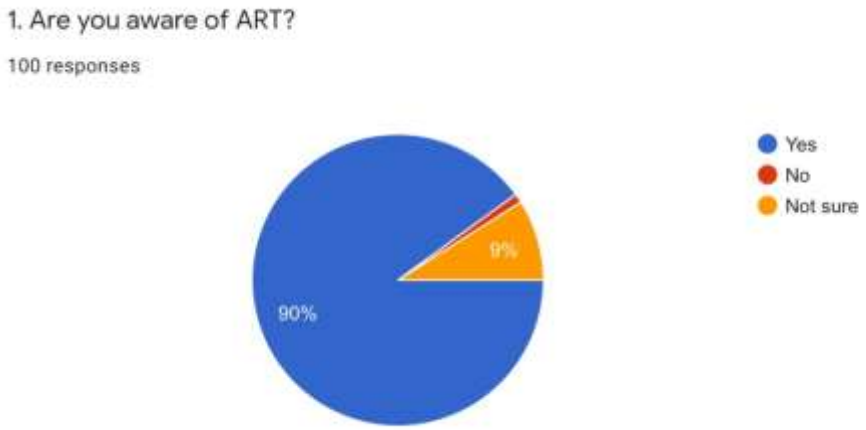
Dental students who were studying 2rd, 3rd year, and final year. Dental students who are not willing to participate were excluded in this study.

QUESTIONNAIRE:

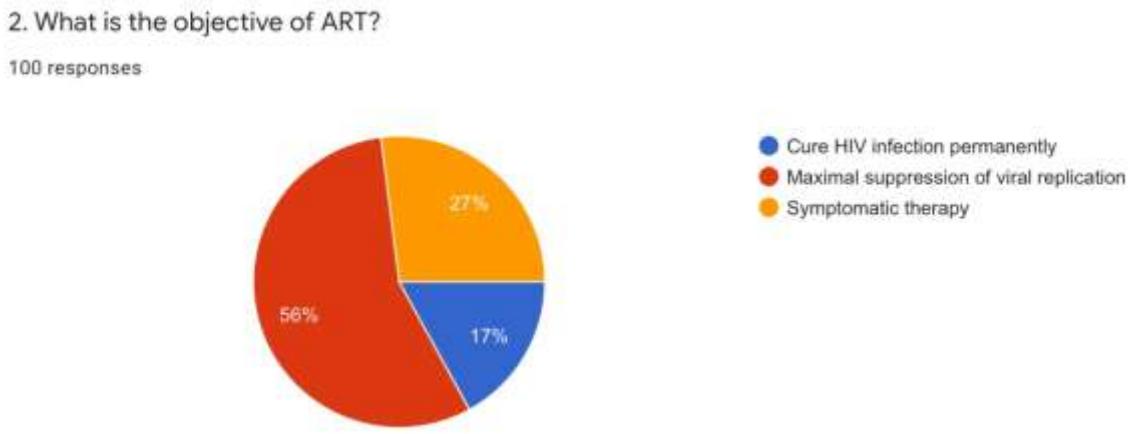
The questionnaire was not targeted at a specific group but all dental students in general to assess their knowledge of antiretroviral drugs prescribed for HIV patients among dental students. A validated questionnaire was distributed among the dental students in this study. This included questions about ART, objectives of ART, group of antiretroviral drugs and newer drug for treating HIV infection. The data extracted were tabulated, statistically analysed and results were obtained using SPSS software.

3. RESULTS:

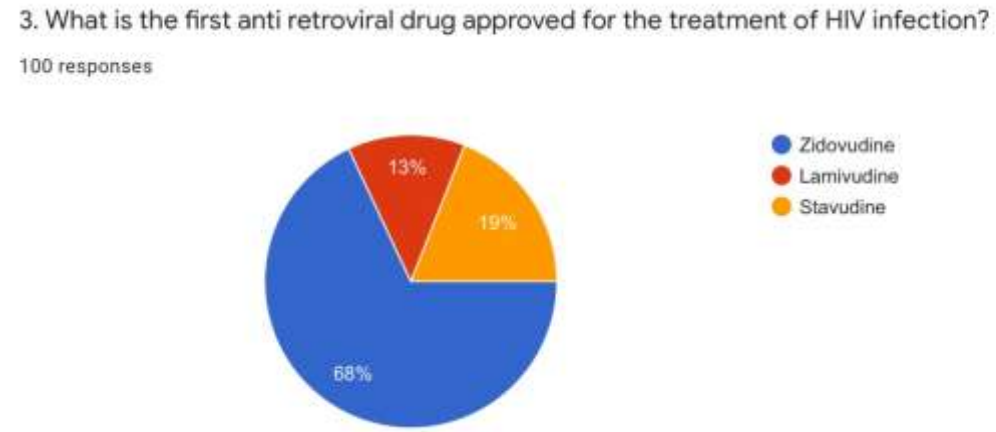
Among the study population, majority (90%) aware of antiretroviral therapy (ART) whereas 9% of the study population not sure about antiretroviral therapy and 1% of the study population not aware of antiretroviral therapy.



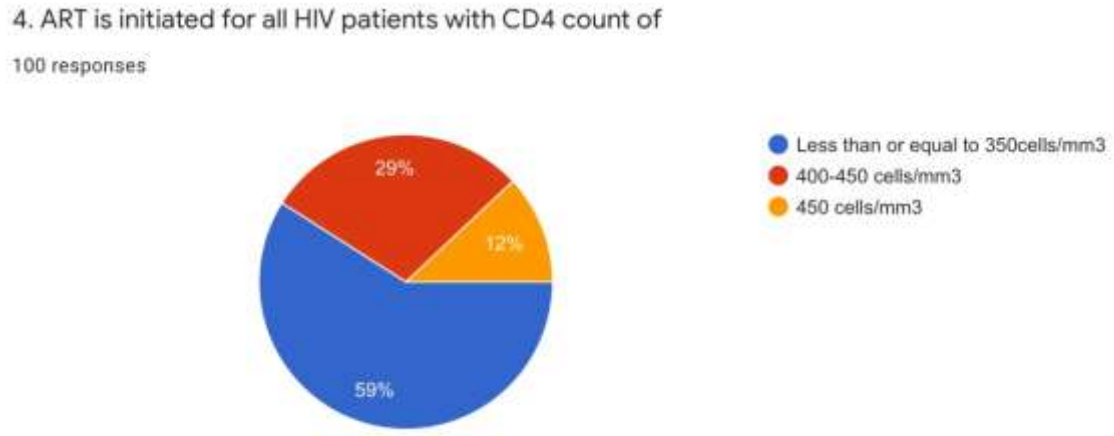
Among the study population, majority (56%) aware that antiretroviral therapy is given to suppress the replication of virus maximally whereas 27% of the study population told that antiretroviral therapy is given to reduce symptoms of HIV infection and 17% of the study population told that antiretroviral therapy is given to cure HIV infection permanently.



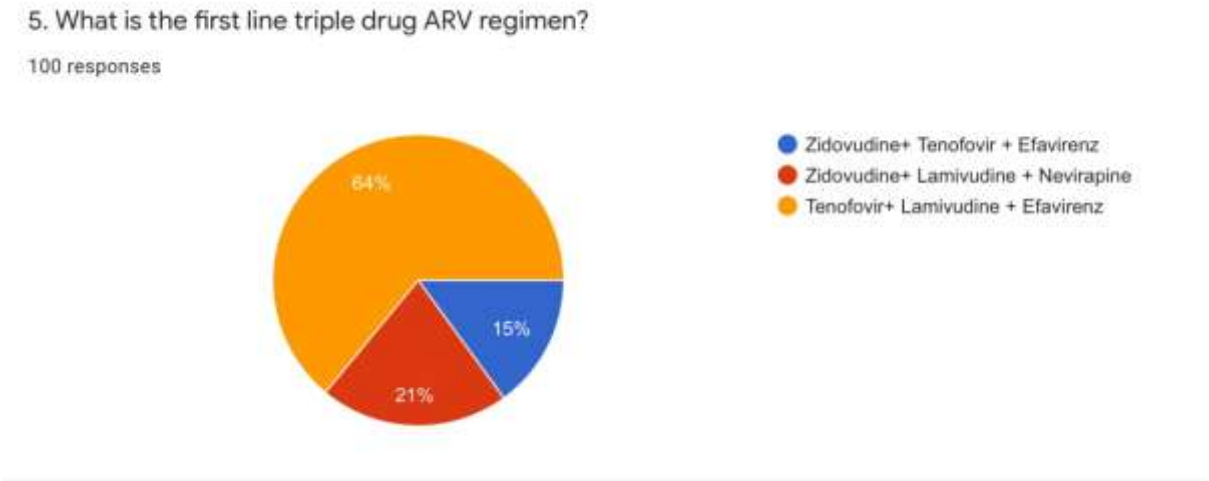
Among the study population, majority (68%) aware that zidovudine is the first antiretroviral drug approved for the treatment of HIV infection, whereas 19% of the study population told that stavudine is the first antiretroviral drug approved for the treatment of HIV infection and 13% of the study population told that Lamivudine is the first antiretroviral drug approved for the treatment of HIV infection.



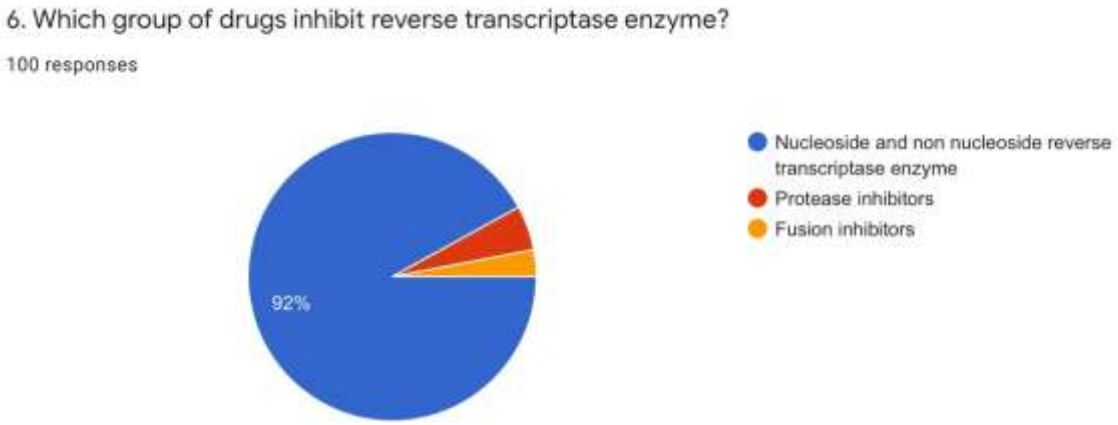
Among the study population, majority (59%) aware that ART is initiated for all HIV patients with CD4 count of less than or equal to 350 cells/mm3 whereas 29% of the study population told that ART is initiated for all HIV patients with CD4 count of 400-450 cells/mm3 and 12% of the study population told that ART is initiated for all HIV patients with CD4 count of 450 cells/mm3.



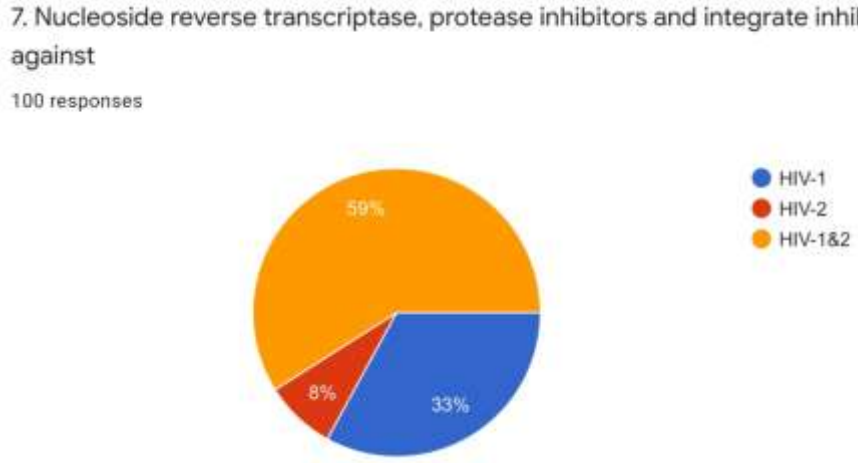
Among the study population, majority (64%) aware that Tenofovir, Lamivudine and Efavirenz is the first line triple drug ARV regimen whereas 21% of the study population told that zidovudine, Lamivudine and nevirapine is the first line triple drug ARV regimen and 15% of the study population told that zidovudine, Tenofovir and Efavirenz is the first line triple drug ARV regimen.



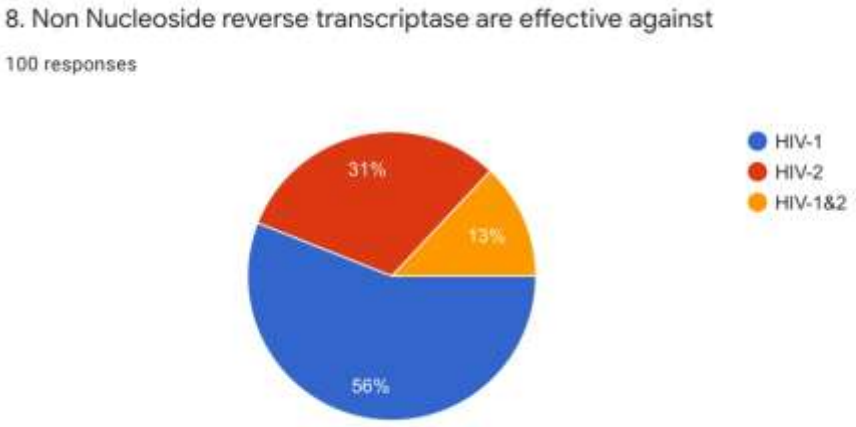
Among the study population, majority (92%) aware that nucleoside and non nucleoside reverse transcriptase enzyme inhibitors were the drugs inhibit reverse transcriptase enzyme whereas 5% of the study population told that protease inhibitors were the drugs that inhibit reverse transcriptase enzyme and 3% of the study population told that fusion inhibitors were the drugs that inhibit reverse transcriptase enzyme.



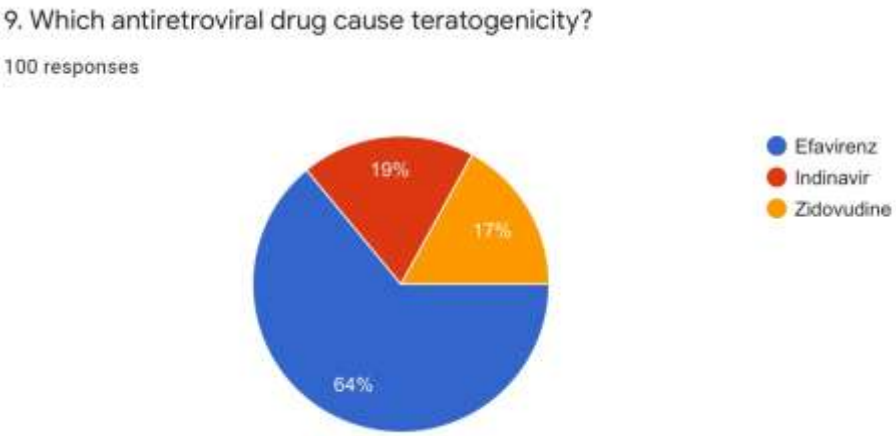
Among the study population, majority (59%) aware that nucleoside reverse transcriptase inhibitors, protease inhibitors and integrase inhibitors are effective against HIV-1&2 whereas 33% of the study population told that nucleoside reverse transcriptase inhibitors, protease inhibitors and integrase inhibitors are effective against HIV-1 and8% of the study population told that nucleoside reverse transcriptase inhibitors, protease inhibitors and integrase inhibitors are effective against HIV-2.



Among the study population, majority (56%) aware that non nucleoside reverse transcriptase inhibitorsare effective against HIV-1 whereas 31% of the study population told that non nucleoside reverse transcriptase inhibitorsare effective against HIV-2 and 13% of the study population told that non nucleoside reverse transcriptase inhibitors are effective against HIV-1&2.

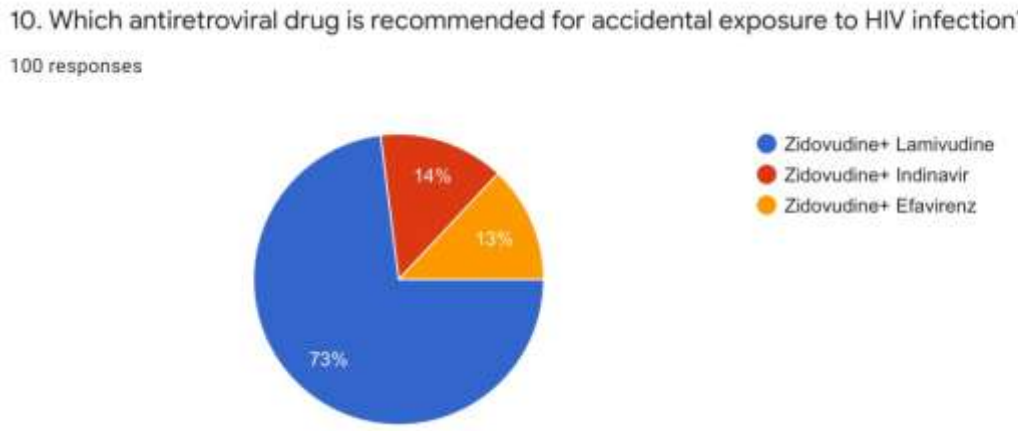


Among the study population, majority (64%) aware that Efavirenzis the antiretroviral drug which causes teratogenicity, whereas 19% of the study population told that indinaviris antiretroviral drug which causes teratogenicity
and 17% of the study population told that zidovudine is the antiretroviral drug which causes teratogenicity.

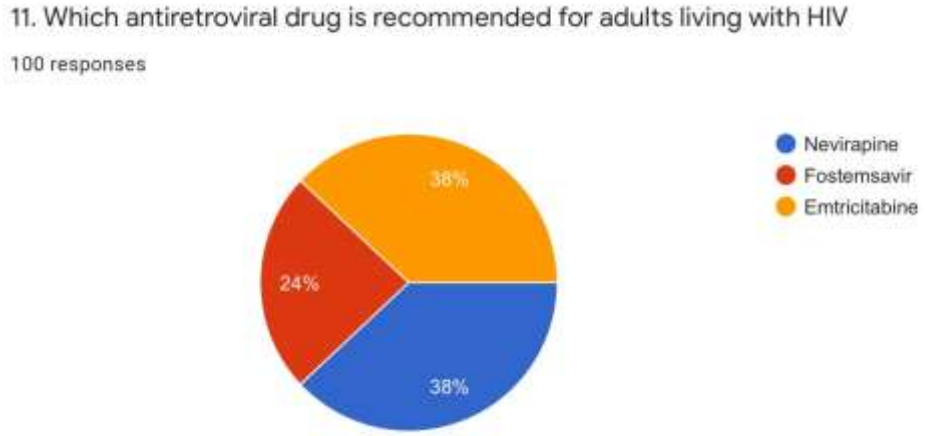


Among the study population, majority (73%) aware that zidovudine and Lamivudine is recommended for accidental exposure to HIV infection, whereas 14% of the study population told thatzidovudine and indinavir is recommended for accidental exposure to HIV infection and 13% of the study population told that zidovudine and efavirenzis recommended for accidental exposure to HIV infection.

Among the study population, majority (38%) told that nevirapine and emtricitabine are the



anti retroviral drug recommended for adults living with HIV who have tried multiple medication and whose HIV infection cannot be successfully treated whereas only 24% of the study population aware of fostemsavir which is prescribed for HIV patients who tried multiple medication and while HIV infection cannot be successfully treated.



4. DISCUSSION:

HIV is a major contributor to the global burden of disease. In 2010, HIV was the leading cause of disability adjusted life years worldwide for people aged 30–44 years, and the fifth leading cause for all ages (24). Global AIDS related deaths peaked at 2·3 million in 2005, and decreased to 1·6 million by 2012 (25). People with HIV have a 50% increased risk of myocardial infarctions than do people without HIV after adjustment for vascular risk factors (26). Liver disease is common, mainly because of coinfection with hepatitis B and C, which share similar routes of transmission with HIV (27).

Antiretroviral therapy refers to the use of pharmacologic agents that have specific inhibitory effects on HIV replication. Antiretroviral agents belongs to six distinct classes of drugs, the nucleoside and nucleotide reverse transcriptase Inhibitors, The non nucleoside reverse transcriptase Inhibitors, The protease Inhibitors, The fusion inhibitors, T he CRR 5 Co receptor antagonistic and The Integrase Inhibitors. Each of these classes of drugs inhibits HIV replication at different stages in HIV life cycle (28). Use of combination antiretroviral therapy (cART) also referred to as highly active

antiretroviral therapy (HAART), resulted in a marked improvement in the prognosis of HIV disease (29). HAART includes the combination of three different types of highly effective anti-HIV-1 drugs, including nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleotide reverse transcriptase inhibitors (NNRTIs) and nonpeptidic viral protease inhibitors (PIs) (30). The goals of treatment are to suppress plasma viremia for as long as possible, to delay the selection of drug resistance mutations, and to preserve immune function. PIs, NRTIs and NNRTIs are associated with potent and durable viral suppression (31).

With combination antiretroviral therapy (cART) regimen, the durability of HIV control is limited by many factors (adherence to treatment, drug toxicity, bioavailability, among the most important). Emergence of HIV-1 drug resistance is an inevitable consequence of antiretroviral therapy (ART) failure (32,33). The use of a combination of potent antiviral drugs leads to a reconstitution of the immune system, which in the short- and in the mid-term is sufficient to radically increase the life expectancy and to markedly reduce the incidence of opportunistic events. Incomplete immune reconstitution and persistent immune system hyperactivation in spite of highly active antiretroviral therapy continue to be a challenge. Accurate quantification of HIV-1 Viral Load (VL) in plasma compartment is an important criterion for disease monitoring and management and has now become a standard method for monitoring HIV-infected patients on antiretroviral therapy (34).

5. CONCLUSION:

The results observed in our study showed that awareness and knowledge of antiretroviral drugs for HIV patients among dental students were high. But Dental students were not aware of fostemsavirwhich is recommended for adults living with HIV who have tried multiple medication and whose HIV infection cannot be successfully treated. Various awareness programs should be conducted to educate more about antiretroviral therapy and newer drugs among the dental students.

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