ABSTRACT
The burden of Human Immunodeficiency Virus (HIV) is greatly attributed to treatment failure and high transmission rates among HIV risk groups such as injection drug users (IDUs). In Kenya and other sub-Saharan African countries, protease inhibitors (PIs) especially Ritonavir boosted Lopinavir (LPV/r) or Atazanavir (ATV/r) are main substitute drugs following first line antiretroviral treatment (ART) failure. However, the circulating protease inhibitor drug resistance mutations (PI-DRMs) are yet to be established among Kenyan IDUs who have been shown to posses high drug resistance (13.8%) to first line ART than the general population. In addition, the social demographic and clinical characteristics associated with development of PI-DRMs among Kenyan IDUs are unknown. This study aimed at determining the frequencies of HIV-1 major and minor PI-DRMs and their socio-demographic and clinical determinants among ART-naive and -experienced IDUs from Mombasa County, Kenya. Mombasa County has the highest IDU related HIV incidence in Kenya who also serve as an epidemiological link of HIV-1 infections and drug resistance to the general Kenyan population. This comparative cross-sectional study targeted HIV positive IDUs from Mombasa County (ART-naive=37; ART-experienced=55). Consenting IDUs were recruited and social-demographic information obtained using questionnaires while body mass index (BMI) determined using weight and height ratios. From the three millilitres of venous blood obtained, CD4+ T-cell counts were determined using BD FACSCalibur and an additional 50μL used to prepare dried blood spots (DBS). HIV-1 viral loads were determined from plasma obtained from centrifugation of the remnant venous blood using Abbott m2000. To determine PI-DRMs, HIV-1 proviral DNA was extracted from DBS and the entire protease gene amplified using gene-specific primers. The amplicons were sequenced using BigDye® chemistries and assembled sequences interpreted using Stanford University HIV drug resistance database (HIVDB). Statistical analysis based on the 76 successfully sequenced samples (ART-naive; n =31 and –experienced; n=45) was conducted using the Chi-square test for comparing proportions between the groups, and Mann-Whitney U test to establish associations between continuous variables. An overall prevalence was 5.3% following detection of three major PI-DRMs [D30N (n=1), D30N+M46I (n=2) and L90M (n=1)] in one (3.2%) ART-naive and three (6.7%) ART-experienced IDUs (p=0.459) which confer resistance to LPV/r and ATV/r. Similarly, nine (29.0%) ART-naive and eight (17.8%) ART-experienced IDUs had minor PI-DRMs (p=0.190) comprising of G48E (n=2), G48R (n=1), K20I (n=2), L10I (n=6), L10V (n=1) and T74S (n=1). Additionally, major PI-DRMs coexisted with minor PI-DRMs and were relatively more in males (75%; p=0.182) and associated with high viral loads (median=175,606, IQR, 38,803-270,810 copies/ml, p=0.04) among ART-experienced IDUs indicating that major PI-DRMs are significant contributors to treatment failure. However, no significant differences were observed in BMI, CD4+ T-cell counts and viral loads among ART-naive and –experienced IDUs with minor PI-DRMs. Collectively, this findings demonstrate that both ART-naive and –experienced IDUs are likely reservoirs of PI-DRMs associated with high viral loads. There is need for PI-DRMs testing prior to regimen switching as well as re-adjust the currently used protease inhibitors in Kenya with more effective PIs.