# Significant fibrosis burden among hepatitis C and human immunodeficiency virus co-infection among injection drug users [IDUs] from Mombasa County, Kenya

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## ABSTRACT

Globally 36.7 million people have HIV, and in Kenya it is estimated that 1.5 million are infected. The HCV burden is estimated to be 32 million in sub Saharan Africa with Kenya having a prevalence of less <1%. In Kenya Injection Drug Users [IDU's] are estimated to be 50,000. There is increased public concern on the rising cases of injection substance users, which has also led to increased HIV prevalence in Mombasa County, which stands at 8.6%. This is above Kenya's prevalence rate, which is at 6.3%. Lymphopaenias among the HIV and HCV co-infected IDU's has also not been explored and therefore this study was aimed to address this gap. Through this study significant fibrosis and lymphopaenias among HIV- and HCV-co-infected injection substance users were determined. While HIV promotes acceleration of HCV infections towards fibrotic liver disease, HCV increases immunosuppression in HIV infections, leading to early acquired immunodeficiency syndrome (AIDS) and death in untreated cases. Liver disease related to hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection may affect the immune status of the injection substance users. Limited data exists on significant fibrosis and lymphopaenia among human immunodeficiency virus and hepatitis C virus co-infected injection drug users. This was a cross-sectional study involving consenting adult (≥18 years) IDUs at Bomu Hospital, Mombasa, Kenya. The study groups were HCV-/HIV- IDUs (n=114); HCV-/HIV+ IDUs (n=73); HCV+/HIV- IDUs (n=19); and HCV+/HIV+ co-infected (n=17). A total of 223 participants were recruited. Socio-demographic and clinical characteristics data were collected using a pre-tested structured participant questionnaire. Consenting participants were serologically screened for the hepatitis C virus and also screened for the human immunodeficiency virus using the national algorithm of testing. Immunological status was tested by the BD FACS Calibur flow cytometer. Immunologic staging was based on the CD4 count, where lymphopaenia was a count of <500 cells/µl. Platelets alongside aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were also determined. The aspartate aminotransferase to platelet ratio index (APRI), fibrosis 4 index (FIB 4) and non-alcoholic fatty liver score (NAFLD) were used to determine significant fibrosis. APRI approached significant difference (P=0.054) across the groups. Age showed significance P 0.001 and gender P<0.0001. The AST levels across the groups are P=0.001. In immunological staging, lymphopaenia was more profound in HIV mono-infected injection drug users (65.8%), HCV/HIV co-infected injection substance users (41.2%), HCV/HIV uninfected (21.1%) and lastly HCV mono-infected injection substance users (15.8%). From the results it can be concluded that HCV/HIV co-infection among IDU's, is associated with high burden of significant fibrosis and lymphopaenia. Significant fibrosis was more pronounced across groups with HCV mono-infected IDUs leading, while lymphopaenia was most severe in HIV mono-infected IDUs (65.8%). The HCV/HIV co-infected burden of both significant fibrosis and lymphopaenia (41.2%) is progressively high. These findings highlight the profound impact of HIV and HCV on liver disease progression and immune suppression. This emphasises the urgent need for early screening, monitoring and integrated management of co-infected individuals to reduce morbidity and mortality in this vulnerable population.

**Key Words:** Biomarker, Co-Infection, Hepatitis C Virus, Injection Drug Users, Kenya, Mombasa County

## I. INTRODUCTION

Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) are transmitted mainly through intravenous route and penetrative sexual intercourse. Globally 37 million people are estimated to be living with HIV (Pandey & Galvani, 2019). The global HIV prevalence is 0.8%. In sub-Saharan Africa an estimated 25.5 million people are living with HIV. A vast majority estimated at 19 million people living with HIV are in East and Southern Africa (Kurth et al., 2015). In Kenya an estimated 1.5 million people are living with HIV. In terms of burden, Kenya is ranked fourth

alongside Mozambique and Uganda. HIV prevalence in Kenya is at 6.3% and 78,000 new infections occur annually (Kurth *et al*., 2015). Mombasa County has a prevalence rate of 8.6%.

Hepatitis C is considered a global issue that mostly affects the developing countries (Roudot-Thoraval, 2021). HCV is a single stranded RNA virus belonging to the family flaviviridae. It has eleven major genotypes with genotype 1 being the most prevalent genotype globally (46%) followed by genotype 3 (22%) and genotype 2 and 4 (13%) each (Dhiman et al., 2016). The global burden of HCV is estimated at 130 – 180 million people. HCV has genotypes 1-11 with a variety of subtypes: a, b, c, and about 100 strains. The most widely distributed genotypes are 1-3 with genotypes 1a and 1b accounting for 60% of infections (Cepeda et al., 2022).

HCV is known to cause both chronic and acute infection in humans. HCV is considered a leading cause of chronic liver disease, the prevalence was lowest in Southern Africa (0.72 %), followed by Eastern Africa at 3.00 %, Western Africa at 4.14 %, and Central Africa at 7.82 %. Blood donors consistently had the lowest prevalence (1.78 %), followed by pregnant women (2.51 %), individuals with comorbid HIV (3.57 %), individuals from the general population (5.41 %), those with a chronic illness (7.99 %), and those at high risk for infection (10.18 %) (Mora et al., 2016).

### 1.1 Statement of the Problem

There is an increased public concern on the rising cases of injection drug users in the country. Injection substance use in the coastal region has been on the rise and this has led to increased prevalence of HIV and HCV. HIV and HCV co-infected injection drug users seem to bear the biggest burden of significant fibrosis and lymphopaenia (Trickey et al., 2019a). This has however not been established in previous studies done. As a result, there is need to address HIV and HCV among the co-infected so as to address the challenges in the diagnosis and management of this disease outcomes.

Significant fibrosis results to the impairment of the liver which results in a number of derangements in the body system which may lead to increased morbidity and mortality to the affected persons. Therefore, with increasing cases of injection drug use in the country together with HCV and HIV co-infection the cases of significant fibrosis could possibly be on the rise and therefore this study was aimed at addressing this gap.

Previous studies (Nelson et al., 2011; Sanvisens et al., 2011) have also shown that there is an association between HIV and lymphopaenia, but little has been done to determine the association between HCV and HIV co-infection, injection drug use and lymphopaenia. HCV infection is known to affect the liver, but in our case, there is also the aspect of injection drug use and HIV. The question that was being addressed by this study was to understand the effect of HCV and HIV co-infection, injection drug use and the progression of HCV and fibrosis.

### 1.2 Research objectives

i. To evaluate the burden of significant fibrosis (APRI >1.5) among HCV/HIV co-infected IDU's in Mombasa County, Kenya.
ii. To determine the prevalence of lymphopaenia (CD4 <500 cells/µl) among HCV/HIV co-infected IDU's in Mombasa County, Kenya.

## II. LITERATURE REVIEW

The global situation of Human immunodeficiency virus (HIV) is that 36.7 million people are living with HIV at the end of 2015 (Mwatelah *et al*., 2015). The risks and incidents of HIV infection remain high among certain demographics globally, including IDU's, commercial sex workers (CSW) and men having sex with men (MSM) (Mwatelah *et al*., 2015).

Recent studies have shown an increase in HCV sero-prevalence over the last decade escalating to 2.8%, corresponding to an average of >185 million infections globally. An estimated 90% of global HCV burden is among the low to medium income countries where Kenya lies in. It has also been globally estimated that only 7% of the HCV diagnosed are initiated on treatment (Wadhva *et al*., 2018). HCV prevalence is at 5.3% and an estimated 32 million people are infected in sub Saharan Africa. Egypt has the highest prevalence in the world which is at 17.5% (Sonderup et al., 2017). In Kenya the prevalence is <1%.

### 2.1 Liver Fibrosis Infection

Fibrosis results from excessive accumulation of scar tissue which leads to inflammation of the liver cells. Microbial components which include lipopolysaccharide (LPS), lipoteichoic acid, and flagellin may promote liver fibrosis by the stimulation of HSCs and Kupffer cells with a LPS binding protein (LBP) and soluble CD14 (sCD14) (Chen et al., 2020).

Needle biopsy of the liver is the gold standard. It is however not risk free, lacks accuracy and many times patients are skeptical about the procedure. Serum biomarkers include single assessment or combined indexes such as

APRI, FIB-4, NAFLD, AST/ALT ratio and Forns index. In this study APRI was used to test for significant fibrosis. APRI is a non-invasive score formula. Imaging modalities may be repeated where necessary. APRI is cheap, better tolerated, safer and more accessible to the patient than liver biopsy (Wang *et al.*, 2017). The aspartate aminotransferase to platelet ratio index (APRI) is recommended by the world health organization (WHO) for the assessment of the presence of liver fibrosis where liver biopsy is unavailable (Wandeler *et al*., 2016).

### 2.2 Platelets

The normal platelet count is 150-450*$10^{9/L}$ with a mean platelet diameter 1-2µ. They normally account for 8-16% of total blood count and they are indirectly related to the state of marrow production (Dinakaran et al., 2024). Platelets are multifunctional cells usually involved in initiation of atheroma, endothelial dysfunction and in the modulation of inflammatory and immune responses in a number of diseases (Hottz et al., 2018). Megakaryocytes transfer to platelets all cellular components responsible for their hemostatic immune functions and this includes granule stored chemokines. Megakaryocytes also display pattern recognition receptors (PRR) and cytokine receptors (Cunin & Nigrovic, 2019).

## III. METHODOLOGY

### 3.1 Study Design and Population

This was a cross-sectional study involving consenting adult IDUs at Bomu Hospital, Mombasa, Kenya. The study population was among consenting injection substance users who are HCV mono-infected, HIV mono-infected and HCV/HIV co-infected.

### 3.2 Study Site

The study area was Mombasa County, Kenya in particular at Bomu Hospital. Mombasa County has a total area of 294.7 $km^2$ where land has an area of 229.7 $Km^2$ and water 65 $Km^{2.}$ The latitude is $3^0$56’ and $4^0$10’ south of equator and the longitudes are $39^0$34’ and $39^0$46$^0$ East.

### 3.3 Sample Size and Sampling Technique

Injection drug users were recruited via respondent- driven sampling (RDS), snowball and targeted street outreach (TSO) sampling method. The Cochran formula was used to determine the minimum sample size as follows:

$N=Z^2PQ/d^2$ $N=\frac{1.96^2 \text{ X } (0.183\text{X}0.817)}{0.05^2}$ =230

Where: N=the minimum sample size required, Z= Confidence level at 95 % (standard value of 1.96), P= prevalence of HIV among IDUs in Kenya of 18.3% (Waimar *et al.*, 2015) and, Q= (100-P)

The HIV prevalence for the HCV/HIV co-infection among PWID in Mombasa County was used since it is known. However, the prevalence of both HCV/HIV co-infection has yet to be established especially in Mombasa County.

### 3.4 Ethical Consideration

This protocol approved by Masinde Muliro University of Science and Technology Institutional Ethical Review Committee (MMUST-IREC) protocol number (MMU/COR: 403012 vol 2 (12). The National Council on Science and Technology (NACOSTI) licence number (NACOSTI/P/18/71025/23382) authorized the study. All participants signed consent forms.

### 3.5 Data Collection

Demographic, clinical, and laboratory data were collected. Clinical chemistry parameters included AST and ALT. Hematological parameters assessed included lymphocytes count, CD3, CD4, CD45 and platelet count.

### 3.6 Statistical Analysis

Data cleaning and coding was done using Microsoft Excel. Data analysis was done by use of SPSS version 20 (SPSS Inc. Chicago, IL). Graph pad prism (version 6) was also used for statistical evaluation of the data. Continuous data (age, laboratory measures) summarized as medians (IQR) and categorical data (gender, duration of injection) presented as proportions were tabulated. Statistical comparisons of the continuous data across the study groups were performed using non-parametric ANOVA (Kruskal Wallis) tests followed by Dunn’s post-hoc corrections for multiple comparisons. The continuous data for significant fibrosis and lymphopaenias was summarized as medians and interquartile range. The medians for significant fibrosis and lymphopaenias were then compared across groups by use of Kruskal-Wallis test followed by Dunn’s post hoc analysis for significant difference. *P* values <0.05 were considered significant.

## IV. FINDINGS & DISCUSSION

### 4.1 Response Rate

A total of 223 adults were recruited into the study. The study participants were categorized into the following four groups: 1) HCV and HIV co-infected (n=17); 2) HCV mono-infected (n=19); 3) HIV mono-infected (n=73) and HCV and HIV uninfected (n=114).

### 4.2 Demographic and Clinical Characteristics of the Study Participants

The demographic and clinical characteristics of the study participants were analyzed to determine significant differences between HCV+/ HIV+ IDU's; HCV-/HIV+ IDU's; HCV+/HIV- IDU's and HCV-/HIV- IDU's. Among the virus infected group, the proportion of males was higher HIV+/HCV+ co-infected IDU's (88.2%) and HCV+/HIV- IDU's (94.7%) compared to HCV-/HIV+ IDU's which had a higher proportion of females (67.1%); the HCV-/HIV- IDU's had a higher proportion of males (90.4%). Age was significantly different across the study groups ($P$=0.001). Subsequent post-hoc analysis showed that age was significantly higher in the HCV+/HIV+ co-infected (P<0.05) and HCV+/HIV- IDU's (P<0.01) relative to the HCV-/HIV+ IDU's group.

The most commonly used narcotic drug in all the study groups was heroin (88.2%, 94.7%, 65.8% and 90.4%) compared to cocaine (11.8%, 0.0%, 31.5% and 7.9%) and concomitant heroin-cocaine injection (0.0%, 5.3%, 2.7% and 1.8%) respectively in the HCV+/HIV+ co-infected IDU's, HCV+/HIV- IDU's; HCV-/HIV+ IDU"s and HCV-/HIV- IDU's group. Other injectable drugs such as diazepam and flunitrazepam were not being abused to a large extent. The use of the sedatives was reported among the study groups. Diazepam (5.9%, 10.5%, 8.2% and 7.0%) and flunitrazepam (0.0%, 10.5%, 0.0% and 4.4%) respectively in the HCV+/HIV+ IDU's; HCV+/HIV- IDU's; HCV-/HIV+ IDU's and HCV-/HIV- IDU's study group. In terms of duration of injection, injection drug users who had injected for ≥1 year had high proportions across all the groups (100%, 84.2%, 87.7% and 57.9%) respective for HCV+/HIV+ IDU's; HCV+/HIV- IDU's; HCV-/HIV+IDU's and HCV-/HIV- IDU's. For the IDU's who had injected drugs for <1 year the proportions were (0.0%, 15.8%, 12.3% and 42.1%) respectively in the HCV+/HIV+ co-infected; HCV+/HIV- IDU's, HCV-/HIV+ IDU's and HCV-/HIV- IDU's.

**Table 1**

*Demographic and Clinical Characteristics of the Study Participants*

| **Characteristic** | **HCV(-)/HIV(-), n=114** | **HCV(-)/HIV (+), n=73** | **HCV(+)/HIV (-), n=19** | **HCV(+)/HIV (+), n=17** | ***P*-Value** |
|---|---|---|---|---|---|
| Age, yrs. | 31.3 (9.4) | 30.1 (86) | 36.3 (12.4)[b] | 34.3 (7.9)[a] | **0.001** |
| Gender, n (%) | | | | | |
| *Female* | 11 (9.6) | 49 (67.1) | 1 (5.3) | 2 (11.8) | - |
| *Male* | 103 (90.4) | 24 (32.9) | 18 (94.7) | 15 (88.2) | |
| *Injection drugs, n (%)* | | | | | |
| Cocaine | 9 (7.9) | 23 (31.5) | 0 (0.0) | 2 (11.8) | - |
| Heroin | 103 (90.4) | 48 (65.8) | 18 (94.7) | 15 (88.2) | |
| Cocaine+Heroin | 2 (1.8) | 2 (2.7) | 1 (5.3) | 0 (0.0) | |
| Others | | | | | |
| Diazepam | 8 (7.0) | 6 (8.2) | 2 (10.5) | 1 (5.9) | - |
| Flunitrazepam | 5 (4.4) | 0 (0.0) | 2 (10.5) | 0 (0.0) | - |
| *Duration of injection, n (%)* | | | | | |
| <1 year | 48 (42.1) | 9 (12.3) | 3 (15.8) | 0 (0.0) | - |
| ≥1 year | 66 (57.9) | 64 (87.7) | 16 (84.2) | 17 (100.0) | |
| *Frequency of injection, n (%)* | | | | | |
| ≤2 times/day | 53 (46.5) | 19 (26.0) | 7 (36.8) | 3 (17.6) | - |
| >2 times/day | 61 (53.5) | 54 (74.0) | 12 (63.2) | 14 (82.4) | |
| *Non-injection drugs, n (%)* | | | | | |
| Bhang | 50 (43.9) | 46 (63.0) | 15 (78.9) | 7 (41.2) | - |
| Brown sugar | 18 (15.8) | 14 (19.2) | 3 (15.8) | 1 (5.9) | - |
| Flunitrazepam | 52 (45.6) | 46 (63.0) | 12 (63.2) | 8 (47.1) | - |
| Diazepam | 1 (0.9) | 1 (1.4) | 0 (0.0) | 0 (0.0) | |
| Cigarettes | 83 (72.8) | 52 (71.2) | 12 (63.2) | 13(76.5) | - |
| Khat | 19 (16.7) | 27 (37.0) | 3 (15.8) | 4 (23.5) | - |
| Cocktail | 24 (21.1) | 39 (53.4) | 6 (31.6) | 6 (35.3) | - |
| Alcohol | 23 (20.2) | 45 (61.6) | 3 (15.8) | 9 (52.9) | - |

AST was significantly different across the study groups (P=0.001). Subsequent post-hoc analysis showed that AST levels were elevated HCV+/HIV- (P=0.001) and HCV-/HIV+ P<0.01 which was relative HCV+/HIV- IDU's. PRI approached significant difference across the study groups *(P*=0.054). The median was (0.46, 0.52, 0.35 and 0.43) respectively for HCV+/HIV+ IDU's; HCV+/HIV- IDU's; HCV-/HIV+ IDU's and HCV-/HIV- IDU's.

Significant fibrosis class II was predominant across all groups (29.4%, 47.4%, 21.9% and 36.8%) and fibrosis class III (0.0%, 5.3%, 6.8% and 3.5%) respectively for HCV+/HIV+ IDU's; HCV+/HIV- IDU's; HCV-/HIV+ IDU's and HCV-/HIV-IDU's. Using the FIB4 biomarker there was no significant difference among the study groups. For Fib4 the negative results were shown (100%, 100%, 98.6% and 98.2%) respectively for HCV+HIV co-infected, HCV+/HIV-IDU's; HCV-/HIV+ IDU's and HCV-/HIV- IDU's group. Fib4 positive (0.0%, 0.0%, 1.4% and 1.8%) respectively for HCV+/HIV+ IDU's; HCV+/HIV- IDU's; HCV-/HIV+ IDU's and HCV-/HIV- IDU's. AFLD biomarker for the groups was (<-1.455) which shows no significant fibrosis across the study groups (100%, 100%, 100% and 100%) respectively for HCV+/HIV+ IDU's, HCV+/HIV- IDU's; HCV-/HIV+ IDU's and HCV-/HIV- IDU's.

**Table 2**

*Prevalence of significant fibrosis*

| **Characteristic** | **HCV(-)/HIV(-), n=114** | **HCV(-)/HIV+), n=73** | **HCV(+)/HIV(-), n=19** | **HCV(+)/HIV(+), n=17** | ***P.* value** |
|---|---|---|---|---|---|
| AST, U/L | 11.0 (11.0) | 9.0 (6.0) | 19.0 (14.0) | 12.0 (7.0) | 0.001 |
| >ULNR | | | | | |
| Platelets ($\times10^3$/ µl) | 259 (103) | 268 (145) | 306 (160) | 296 (104) | 0.079 |
| <150×$10^3$/µl | | | | | |
| APRI, median (IQR) | 0.43 (0.51) | 0.35 (0.35) | 0.52 (0.31) | 0.46 (0.22) | 0.050 |
| Significant fibrosis, n (%) | | | | | |
| Class I | 68 (59.6) | 52 (71.2) | 9 (47.4) | 12.0 (70.6) | - |
| Class II | 42 (36.8) | 16 (21.9) | 9 (47.4) | 5.0 (29.4) | |
| Class III | 4 (3.5) | 5 (6.8) | 1 (5.3) | 0.0 (0.0) | |
| Fib 4 | 0.25 (0.20) | 0.24 (0.20) | 0.32 (0.24) | 0.27 (0.18) | 0.108 |
| Negative<br>Positive | 112 (98.2)<br>2 (1.8) | 72 (98.6)<br>1 (1.4) | 19 (100)<br>0 (0.0) | 17 (100.0)<br>0 (0.0) | - |
| NAFLD<br>< 1.455 | -71.65 (17.17)<br>114 (100.0) | -70.00 (12.85)<br>73 (100.0) | -83.00 (28.1)<br>19 (100) | -80.91 (15.3)<br>17 (100) | < 0.0001<br>- |

Platelet absolute count (*$10^6$/ul) showed no significance difference among the medians (104, 160,145 and 103) respectively for HCV+/HIV+ IDU's; HCV+/HIV- IDU's; HCV-/HIV+ IDU's and HCV-/HIV- IDU's. This suggests that there is increased need to combine different markers for better diagnosis of significant fibrosis. Data shown are median (IQR) for AST and platelet and proportion for other categorical variables. AST, aspartate aminotransferase; APRI, aspartate aminotransferase to platelet ratio index (%). HCV+/HIV+, HCV+/HIV-, HCV-/HIV+ and HCV-/HIV- study groups. APRI <0.5, Class I; APRI ≥0.5<1.5, Class II and APRI >1.5, Class III.

Absolute lymphocytes were approaching significance across the study groups (P=0.05). Subsequent post-hoc analysis showed that absolute lymphocytes were elevated in HCV-/HIV+ (P=0.001) which was relative HCV-/HIV- individuals. CD45 absolute count showed significance across the study groups (P=0.001). Subsequent post-hoc analysis showed that CD45 absolute count was significantly higher in the HCV-/HIV+ (P=0.001) relative to the HCV-/HIV- individuals. CD3+CD45 absolute count showed significance across the study groups (P=0.05). Post hoc analysis showed CD3+CD45 was significantly increased in HCV-/HIV+ (P=0.05) as compared to HCV-/HIV-study individuals.

**Table 3**

*Lymphocyte and lymphopaenia levels*

| **Characteristic** | **HCV(-)/HIV(-), n=114** | **HCV(-)/HIV+), n=73** | **HCV(+)/HIV(-), n=19** | **HCV(+)/HIV(+), n=17** | ***P.* value** |
|---|---|---|---|---|---|
| Lymphocytes ×$10^3$/µl | 2.4 (1.1) | 2.2 (1.9) | 2.1 (1.2) | 2.4 (1.3) | 0.021 |
| Lymphocytes % | 37.0 (15.2) | 38.3 (19.0) | 32.5 (14.7) | 36.3 (14.4) | 0.250 |
| Lymphopenia, n (%) | 14 (12.3) | 18 (24.7) | 5 (26.3) | 2 (11.8) | - |
| CD45+µ/l | 1982 (1229) | 2410 (1062) | 1685 (972) | 2265 (1541) | <0.0001 |
| CD3+CD45+×$10^3$/µl l | 1682 (1020) | 1609 (1424) | 1342 (864) | 1724.5 (1012) | 0.001 |
| CD3+CD4+CD45+×$10^3$/µl | 23 (9) | 31 (11) | 21 (16) | 36 (13.3) | 0.001 |
| CD3+CD4+ T cells ×$10^3$/µl | 515 (1179) | 891 (725) | 337 (352) | 938 (641) | <0.0001 |
| CD3+CD4+ T cells % | 78 (9.5) | 73 (9) | 72 (14) | 71 (13) | 0.031 |
| **Immunological staging** | | | | | |
| Stage 1 | 5 (4.4) | 18 (24.7) | 0 (0.0) | 0 (0.0) | |
| Stage 2 | 19 (16.7) | 30 (41.1) | 3 (15.8) | 7 (41.2) | |
| Stage 3 | 90 (78.9) | 25 (34.2) | 16 (84.2) | 10 (58.8) | |

Data are presented as numbers (n) and proportions (%). HCV+/HIV+, HCV+/HIV-, HCV-/HIV+ and HCV-/HIV- study groups. Stage 1 CD4+T cell <200; stage 2 ≥200<500 and stage 3 ≥500.

### 4.3 Discussion

Both AST and ALT may be used as indicators for liver damage or injury as a result of different types of disease conditions. Although it's not specific it can be used with other markers to diagnose significant fibrosis. Chronic HCV infection may result in slight elevation of both AST and ALT enzymes, these results in liver injury and even cirrhosis (Tamber et al., 2023).

With injecting drugs, this could possibly be aggravated and disease prognosis will be poor. This has been shown in other studies that injecting drugs raises the AST levels (Marks et al., 2022). AST was significantly elevated (P=0.001) among HCV+/HIV- PWID relative to the HCV-/HIV+ individuals. AST was also significantly elevated (P=0.05) in HCV-/HIV+ PWID compared to HCV-/HIV- individuals. This results correlates to a study by Langohr et al on liver enzyme alteration in HCV mono-infected and HCV+/HIV+ co-infected patients (Langohr et al., 2008).

The same elevated AST level was seen in HCV-/HIV+ IDU's. These may be attributed to the fact that HIV lowers person's immunity and as a result of injecting drugs e.g. cocaine, the effect of the drug may include and not limited to liver damage (Busca et al., 2022). APRI proved reliable in the diagnosis of significant fibrosis with median values and proportions ≥0.5 in the HCV+/HIV- IDU's. Despite the availability of a number of validated non-invasive indices such as FIB4 and APRI to aid in the evaluation of significant fibrosis, liver biopsy remains the gold standard for diagnosis (Wang *et al*., 2017). Although relatively safe the procedure is costly and not without risk.

APRI was used in this study and it has been proven to be reliable in a number of previous studies (Li *et al*., 2017). In this study we found out that platelet count, AST level and ALP levels were independent predictors of significant fibrosis (Wadhva *et al*., 2018). APRI class I <0.5 the average proportion was over 50% apart from the HCV+/HIV-IDU's where it stood at 47.4%. APRI class II was highest in the HCV+/HIV- IDU's however in APRI class III it was <7% across all the groups. APRI class II and class III combined had significant high proportion among the various groups; HCV+/HIV+ IDU's comprised 29%; HCV+/HIV- IDU's 54%; HCV-/HIV+ IDU's 29% and HCV-/HIV- IDU's at 40%. These could be as a result of injecting drugs which have an impact in bringing about liver degeneration.

Stage I (<200 CD4 T cells) was observed among the HCV-/HIV+ IDU's with a proportion of 24.7%. Our data also shows that <50% of the HCV-/HIV+ IDU's had CD4 T cell of ≥500. HCV+/HIV+ IDU's also showed reduced proportion of CD4 T cells with a majority (41.2%); HCV-/HIV+ IDU's (41.1%) at the intermediate stage i.e. stage II. The lymphopenia % among the HCV+/HIV+ IDU's (11.8%); HCV+/HIV-IDU's (26.3%); HCV-/HIV+ IDU's (24.7%) and HCV-/HIV- IDU's (12.3%). In the study (41.2%) had a CD4 count of <500 cells/ microl in the HCV+/HIV+ IDU's. These results corresponds with the study done by Singh et al on clinic-haematological profile and its correlation with CD4 counts and other related studies (Aleknavičiūtė-Valienė & Banys, 2022).

With lowered immunity, there is an increased risk of developing immune deficiency among IDU's who are more prone to multiple infections, particularly to HCV and HIV that share similar immune target cells (Waimar et al., 2015). Class III fibrosis was at 3.5% in the HCV-/HIV- IDU's as compared to the HCV+/HIV+ co-infected IDU's this may be associated with polydrug use of the various injectable drugs such as cocaine, heroin, flunitrazepam and diazepam which are all opioids. Opiate drug use through interactions with specific receptors has been shown to modulate antibody response, natural killer cell activity, T-cell development and expression of cytokines and chemokines both in vitro and in vivo. Initiation of HSC activation is associated with increase in several inflammatory cytokines which modulate collagen expression, including TGFβ1, TNFα, IL-1β and IL-6. Specifically, in HSCs, TNFα and IL-6 induce cellular trans-differentiation and activation, ultimately resulting in secretion of pro-fibrotic and proliferative factors, culminating in fibrosis. Since HCV and HIV have similar routes of transmission, co-infection in IDU's is common. This association is linked to long-term morbidity and mortality which is more than in mono-infection of either HCV or HIV.

## V. CONCLUSION & RECOMMENDATION

### 5.1 Conclusion

This study has shown that there is high prevalence of significant fibrosis (29.4%) among HCV+/HIV+ IDU's. This correlates with a study done by Sanvisens et al where significant fibrosis (9.2% to 17.3%) among the co-infected IDU's. The estimation of significant fibrosis by use of non-invasive biomarkers may be helpful with clinical decisions to facilitate access to treatment of chronic HCV and significant fibrosis. These study highlights a substantial burden of significant fibrosis (29.4%) and CD4 based immunosuppression (41.2%) among PWID co-infected with HCV+/HIV+. The high prevalence of fibrosis underscores the urgency of early screening and treatment interventions. These findings reinforce the importance of integrated care models targeting both liver health and immunologic recovery in HCV+/HIV+ co-infected PWID; aiming to reduce morbidity and improve long term outcomes.

### 5.2 Recommendation

It is necessary to scale up HIV and HCV diagnosis particularly in the IDU's population. There should be early initiation of DAA treatment, combined with improved testing, linkage to care and adherence. This will reduce HCV prevalence, significant fibrosis and morbidity among PWID. HCV+/HIV+ co-infected IDU's should be assessed for significant fibrosis by use of non-invasive biomarkers (APRI, FIB-4). In cases of advanced significant fibrosis or cirrhosis, HCC should be monitored to avoid having severe outcomes (Busca et al., 2022). Counseling services should also be enhanced so as to be able to make more IDU's to come out and seek therapeutic and treatment services. There should be comprehensive addiction care to PWID and are HCV+/ HIV+. There is need to combine behavioral, socio-demographic and serological data to inform the planning and implementation of effective prevention and intervention strategies.

## CONFLICT OF INTEREST

None of the authors have a conflict of interest as part of this study.

## REFERENCES


Aleknavičiūtė-Valienė, G., & Banys, V. (2022). Clinical importance of laboratory biomarkers in liver fibrosis. *Biochemia Medica, 32*(3), 346–356. https://doi.org/10.11613/BM.2022.030501

Busca, C., Sánchez-Conde, M., Rico, M., Rosas, M., Valencia, E., Moreno, A., Moreno, V., Martín-Carbonero, L., Moreno, S., Pérez-Valero, I., Bernardino, J. I., Arribas, J. R., González, J., Olveira, A., Castillo, P., Abadía, M., Guerra, L., Mendez, C., & Montes, M. L. (2022). Assessment of noninvasive markers of steatosis and liver fibrosis in human immunodeficiency virus-monoinfected patients on stable antiretroviral regimens. *Open Forum Infectious Diseases, 9*(7), ofac279. https://doi.org/10.1093/ofid/ofac279

Cepeda, J. A., Thomas, D. L., Astemborski, J., Rudolph, J. E., Gicquelais, R., Kirk, G. D., & Mehta, S. H. (2022). Impact of hepatitis C treatment uptake on cirrhosis and mortality in persons who inject drugs. *Annals of Internal Medicine, 175*(8), 1083–1091. https://doi.org/10.7326/M21-3846

Chen, X., Liu, X., Duan, S., Tang, R., Zhou, S., Ye, R., Yang, Y., Wang, J., Yao, S., & He, N. (2020). Plasma inflammatory biomarkers associated with advanced liver fibrosis in HIV–HCV-coinfected individuals. *International Journal of Environmental Research and Public Health, 17*(24), Article 24. https://doi.org/10.3390/ijerph17249474

Cunin, P., & Nigrovic, P. A. (2019). Megakaryocytes as immune cells. *Journal of Leukocyte Biology, 105*(6), 1111–1121. https://doi.org/10.1002/JLB.MR0718-261RR

Dhiman, R. K., Satsangi, S., Grover, G. S., & Puri, P. (2016). Tackling the hepatitis C disease burden in Punjab, India. *Journal of Clinical and Experimental Hepatology, 6*(3), 224–232. https://doi.org/10.1016/j.jceh.2016.09.005

Dinakaran, P., Rajkumar, A., Mohan, N., Parthasarathy, S., & Jayaraman, V. (2024). Evaluation of platelet counts and associated factors using statistical methods. *2024 First International Conference on Innovations in Communications, Electrical and Computer Engineering (ICICEC), 7*(4), 1–9. https://doi.org/10.1109/ICICEC62498.2024.10808228

Hottz, E. D., Bozza, F. A., & Bozza, P. T. (2018). Platelets in immune response to virus and immunopathology of viral infections. *Frontiers in Medicine, 5*(8), 45. https://doi.org/10.3389/fmed.2018.00121

Kurth, A. E., Cleland, C. M., Des Jarlais, D. C., Musyoki, H., Lizcano, J. A., Chhun, N., & Cherutich, P. (2015). HIV prevalence, estimated incidence, and risk behaviors among people who inject drugs in Kenya. *Journal of Acquired Immune Deficiency Syndromes, 70*(4), 420–427. https://doi.org/10.1097/QAI.0000000000000769

Langohr, K., Sanvisens, A., Fuster, D., Tor, J., Serra, I., Rey-Joly, C., Rivas, I., & Muga, R. (2008). Liver enzyme alterations in HCV-monoinfected and HCV/HIV-coinfected patients. *The Open AIDS Journal, 2*, 82–88. https://doi.org/10.2174/1874613600802010082

Li, Q., Ren, X., Lu, C., Li, W., Huang, Y., & Chen, L. (2017). Evaluation of APRI and FIB-4 for noninvasive assessment of significant fibrosis and cirrhosis in HBeAg-negative CHB patients with ALT ≤ 2 ULN: A retrospective cohort study. *Medicine, 96*(12), e6336. https://doi.org/10.1097/MD.0000000000006336

Marks, L. R., Nolan, N. S., Liang, S. Y., Durkin, M. J., & Weimer, M. B. (2022). Infectious complications of injection drug use. *Medical Clinics, 106*(1), 187–200. https://doi.org/10.1016/j.mcna.2021.08.006

Mora, N., Adams, W. H., Kliethermes, S., Dugas, L., Balasubramanian, N., Sandhu, J., Nde, H., Small, C., Jose, J., Scaglione, S., & Layden, J. E. (2016). A synthesis of hepatitis C prevalence estimates in Sub-Saharan Africa: 2000–2013. *BMC Infectious Diseases, 16*(1), 283. https://doi.org/10.1186/s12879-016-1584-1

Mwatelah, R. S., Lwembe, R. M., Osman, S., Ogutu, B. R., Aman, R., Kitawi, R. C., Wangai, L. N., Oloo, F. A., Kokwaro, G. O., & Ochieng, W. (2015). Co-infection burden of hepatitis C virus and human immunodeficiency virus among injecting heroin users at the Kenyan Coast. *PLoS ONE, 10*(7), e0132287. https://doi.org/10.1371/journal.pone.0132287

Nelson, P. K., Mathers, B. M., Cowie, B., Hagan, H., Des Jarlais, D., Horyniak, D., & Degenhardt, L. (2011). Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: Results of systematic reviews. *Lancet, 378*(9791), 571–583. https://doi.org/10.1016/S0140-6736(11)61097-0

Pandey, A., & Galvani, A. P. (2019). The global burden of HIV and prospects for control. *The Lancet HIV*, *6*(12), e809–e811. https://doi.org/10.1016/S2352-3018(19)30230-9

Roudot-Thoraval, F. (2021). Epidemiology of hepatitis C virus infection. *Clinics and Research in Hepatology and Gastroenterology*, *45*(3), 101596. https://doi.org/10.1016/j.clinre.2020.101596

Sanvisens, A., Fuster, D., Serra, I., Tor, J., Tural, C., Rey-Joly, C., & Muga, R. (2011). Estimated liver fibrosis and its impact on all-cause mortality of HCV-monoinfected and HCV/HIV-coinfected drug users. *Current HIV Research*, *9*(4), 256–262. https://doi.org/10.2174/157016211796320298

Sonderup, M. W., Afihene, M., Ally, R., Apica, B., Awuku, Y., Cunha, L., Dusheiko, G., Gogela, N., Lohouès-Kouacou, M.-J., Lam, P., Lesi, O., Mbaye, P. S., Musabeyezu, E., Musau, B., Ojo, O., Rwegasha, J., Scholz, B., Shewaye, A. B., Tzeuton, C., … Spearman, C. W. (2017). Hepatitis C in sub-Saharan Africa: The current status and recommendations for achieving elimination by 2030. *The Lancet Gastroenterology & Hepatology*, *2*(12), 910–919. https://doi.org/10.1016/S2468-1253(17)30249-2

Tamber, S. S., Bansal, P., Sharma, S., Singh, R. B., & Sharma, R. (2023). Biomarkers of liver diseases. *Molecular Biology Reports*, *50*(9), 7815–7823. https://doi.org/10.1007/s11033-023-08666-0

Trickey, A., Fraser, H., Lim, A. G., Peacock, A., Colledge, S., Walker, J. G., Leung, J., Grebely, J., Larney, S., Martin, N. K., Hickman, M., Degenhardt, L., May, M. T., & Vickerman, P. (2019). The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: A modelling study. *The Lancet Gastroenterology & Hepatology*, *4*(6), 435–444. https://doi.org/10.1016/S2468-1253(19)30085-8

Wadhva, R. K., Haque, M. M., Luck, N. H., Tasneem, A. A., Abbas, Z., & Mubarak, M. (2018). Diagnostic accuracy of aspartate aminotransferase to platelet ratio index and fibrosis 4 scores in predicting advanced liver fibrosis in patients with end-stage renal disease and chronic viral hepatitis: Experience from Pakistan. *Journal of Translational Internal Medicine*, *6*(1), 38–42. https://doi.org/10.2478/jtim-2018-0008

Waimar, T., Meredith, S., Dita, B., Jerry, O., Nicholas, M., Fisher, R. H., Helgar, M., Andrea, K. A., Mercy, M., & Scott, G. (2015). HIV and STI prevalence and injection behaviors among people who inject drugs in Nairobi: Results from a 2011 bio-behavioral study using respondent-driven sampling. *AIDS and Behavior*, *19*(Suppl 1), 24–35. https://doi.org/10.1007/s10461-014-0936-3

Wandeler, G., Mulenga, L., Vinikoor, M. J., Kovari, H., Battegay, M., Calmy, A., Cavassini, M., Bernasconi, E., Schmid, P., Bolton-Moore, C., Sinkala, E., Chi, B. H., Egger, M., Rauch, A., & IeDEA-Southern Africa and the Swiss HIV Cohort Study. (2016). Liver fibrosis in treatment-naïve HIV-infected and HIV/HBV co-infected patients: Zambia and Switzerland compared. *International Journal of Infectious Diseases, 51*, 97–102. https://doi.org/10.1016/j.ijid.2016.08.028

Wang, H.-W., Peng, C.-Y., Lai, H.-C., Su, W.-P., Lin, C.-H., Chuang, P.-H., Chen, S.-H., Chen, C.-H., Hsu, W.-F., & Huang, G.-T. (2017). New noninvasive index for predicting liver fibrosis in Asian patients with chronic viral hepatitis. *Scientific Reports, 7*, Article 3589. https://doi.org/10.1038/s41598-017-03589-w