Genotypic Characterization of Hepatitis C Virus from the Patients of a Tertiary Care Hospital in Kathmandu

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Introduction

- Causes acute and chronic hepatitis

Establishes a state of chronic infection in upto 85% of acutely infected patients(Westbrook & Dusheiko, 2014)

- Up to 80% are asymptomatic
  15-30% patients develop cirrhosis or cancer (WHO, 2022)

- Bloodborne & IDU is the most common route of transmission (Flamm, Parker & Chopra, 1998; CDC, 2016)

HCV Prevalence

Global (WHO, 2024)

Infection	Death	
50 Million	242,000	Worldwide
12 M		East Mediterranean regions
9 M		European regions
9 M		South East Asia
7 M		Western Pacific Region
8 M		African Region
5 M		Americas Region

Nepal

Infection	
120,000	DoHS, 2015
0.3- 1.7%	Shrestha et al.,1998; Singh, 1998; Sawayama et al., 1999; Shrestha, 2003; Shrestha, 2006; Sherchand, 2017

Rationale of the Study

- Genotype 1 is the most prevalent genotype.

(Messina et al., 2015)

Distribution of HCV genotypes and sub-genotypes varies.

In Nepal, there is a few genotyping studies.

- No vaccine

Drugs targeting NS3/4A protease, NS5B polymerase and NS5A replication complex of HCV genome

Mutations may develop resistance.

(Kliemann et al., 2016)

Studies on evaluations of mutations at these target sites have not been done so far in Nepal.

Objective of the Study

To identify the HCV genotypes and antiviral drugs target gene mutations in the HCV genome.

Research Design & Methodology

Type of Study

Hospital based cross sectional study

Study Site

- TU TeachingHospital Maharajgunj, Kathmandu
- Central Department of Microbiology, TU
- Norwegian Institute of Public Health, Norway

Target Population

Clinically suspected hepatitis patients

Research Design & Methodology

Sampling Method & Sample Size

Purposive sampling of 103 patients (P=1.7%, e=2.5%) with HCV Ab +ve (Sherchand, 2017)

Duration of Study

:Five Years

Inclusion Criteria

Patients with HCV Ab Positive

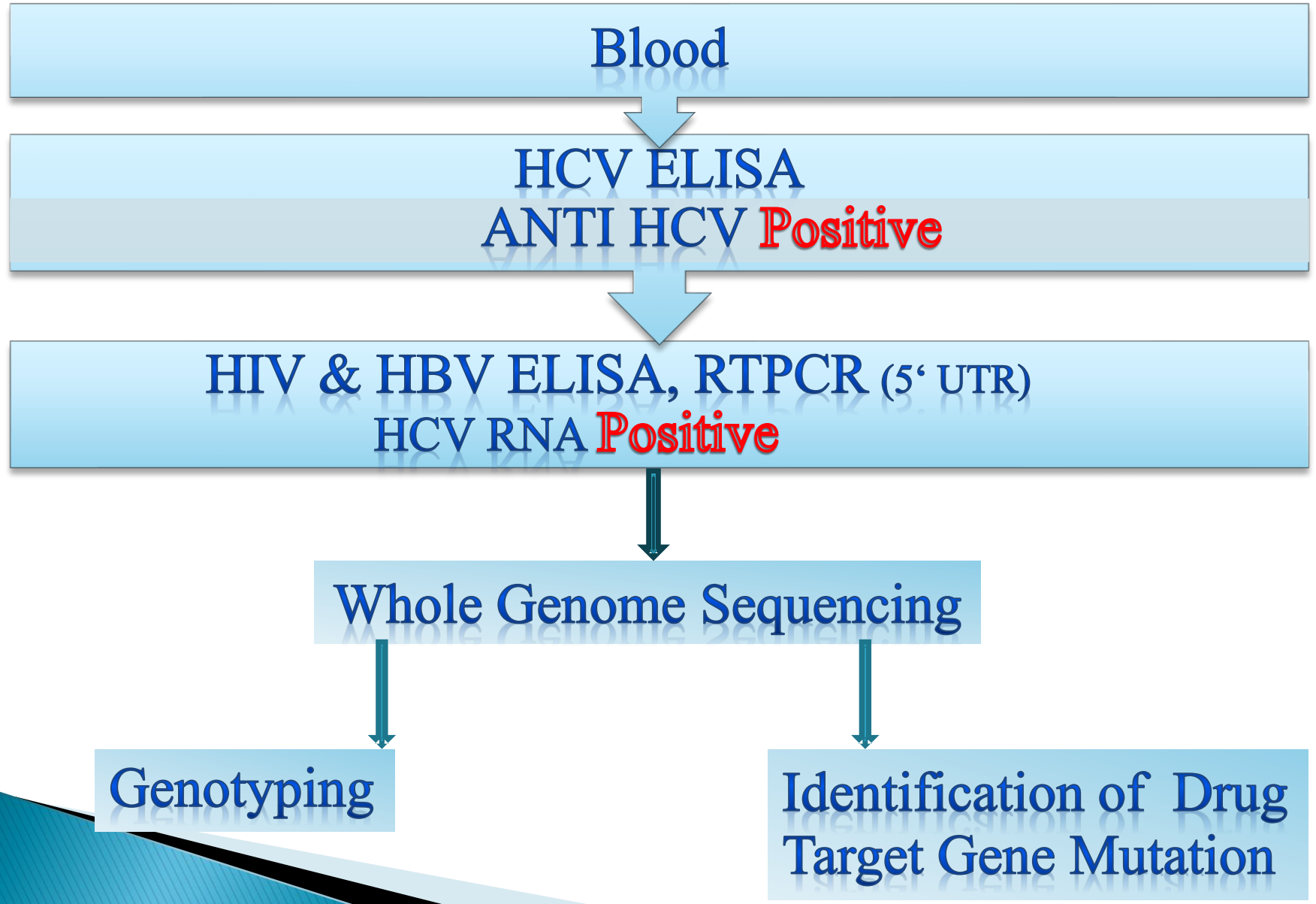
Exclusion Criteria

- Have major psychiatric problems
- Refuse to participate in the study
- Undergoing treatment for HCV

Tools & Techniques

Laboratory investigations & semi structured questionnaire

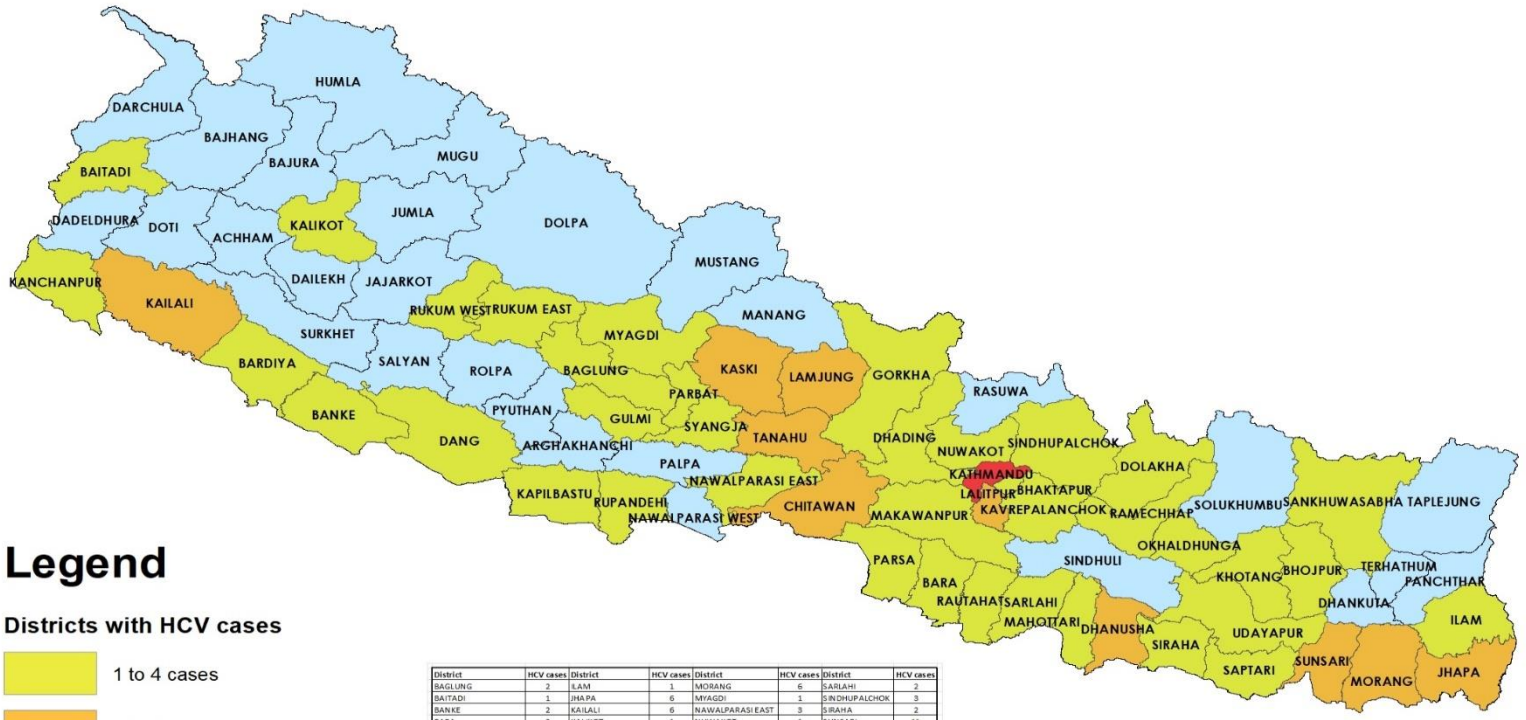
Laboratory Investigations



Results

Geographical Distribution of the Patients

District-Wise Distribution of Hepatitis-C Cases



Legend

Districts with HCV cases

- 1 to 4 cases
- 5 to 11 cases
- More than 11 cases
- Districts with No reported cases

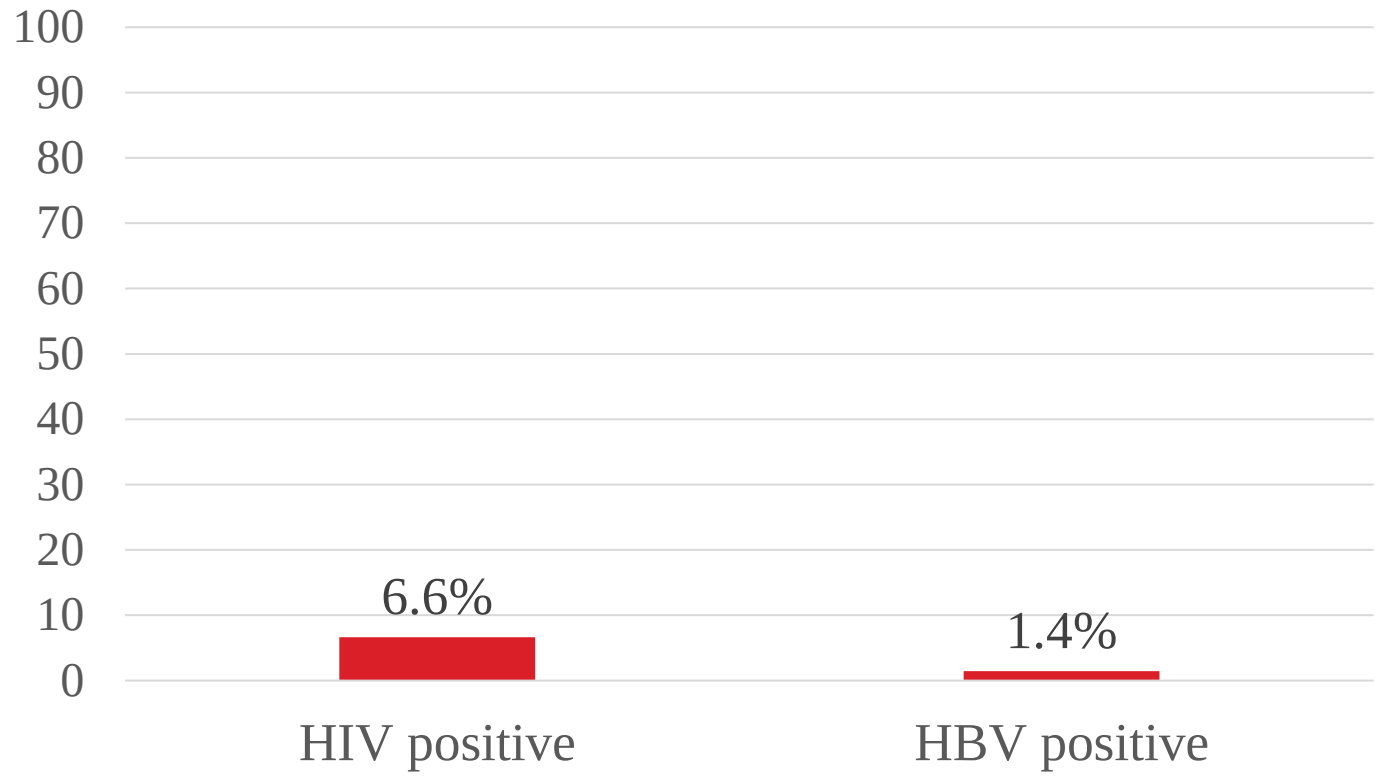
District	HCV cases	District	HCV cases	District	HCV cases	District	HCV cases
BAGLUNG	2	ILAM	1	MORANG	6	SARLAHI	2
BAITADI	1	JHAPA	6	MYAGDI	1	SINDHUPALCHOK	3
BANKE	2	KAILALI	6	NAWALPARASI EAST	3	SIRAHA	2
BARA	2	KALIKOT	1	NUWAKOT	1	SUNSARI	11
BARDIYA	1	KANCHANPUR	4	OKHALDHUNGA	3	SYANGJA	3
BHAKTAPUR	2	KAPILBASTU	2	PARBAT	2	TANAHU	6
BHOJPUR	1	KASKI	8	PARSA	4	UDAYAPUR	1
CHITAWAN	11	KATHMANDU	63	RAMECHHAP	2		
DANG	1	KAVREPALANCHOK	2	RAUTAHAT	2		
DHADING	3	KHOTANG	4	RUKUM WEST	1		
DHANUSHA	5	LALITPUR	9	RUKUM EAST	1		
DOLAKHA	2	LAMJUNG	6	RUPANDEHI	1		
GORKHA	2	MAHOTTARI	3	SANKHUWASABHA	1		
GULMI	1	MAKAWANPUR	3	SAPTARI	1		

Seroprevalence of HCV (0.84%, 211/25133) N=211

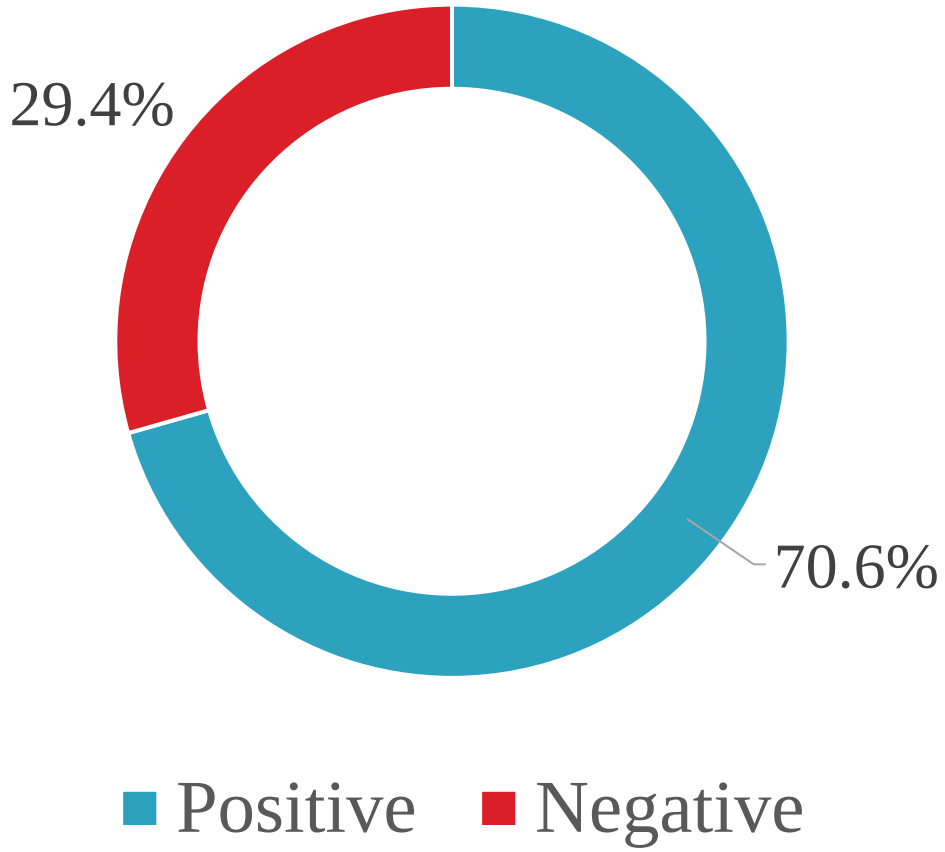
Variables		Number (N)	Positive (N)	Prevalence %	P-value
Sex	Male	12980	174	1.34	<.001
	Female	12148	37	0.30	
Caste	Brahmin/Chhetri	11798	69	0.58	
	Dalit	1776	14	0.79	
	Janajati	8591	105	1.22	<.001
	Madeshi	2045	19	0.93	
	Thakuri	589	4	0.68	
Age	Paediatric group (0-14 yrs)	882	1	0.11	
	Young group (15-47 yrs)	15107	156	1.03	<.001
	Middle age group (48-63 yrs)	5784	48	0.83	
	Elderly group (≥64 yrs)	3360	6	0.18	

N=211

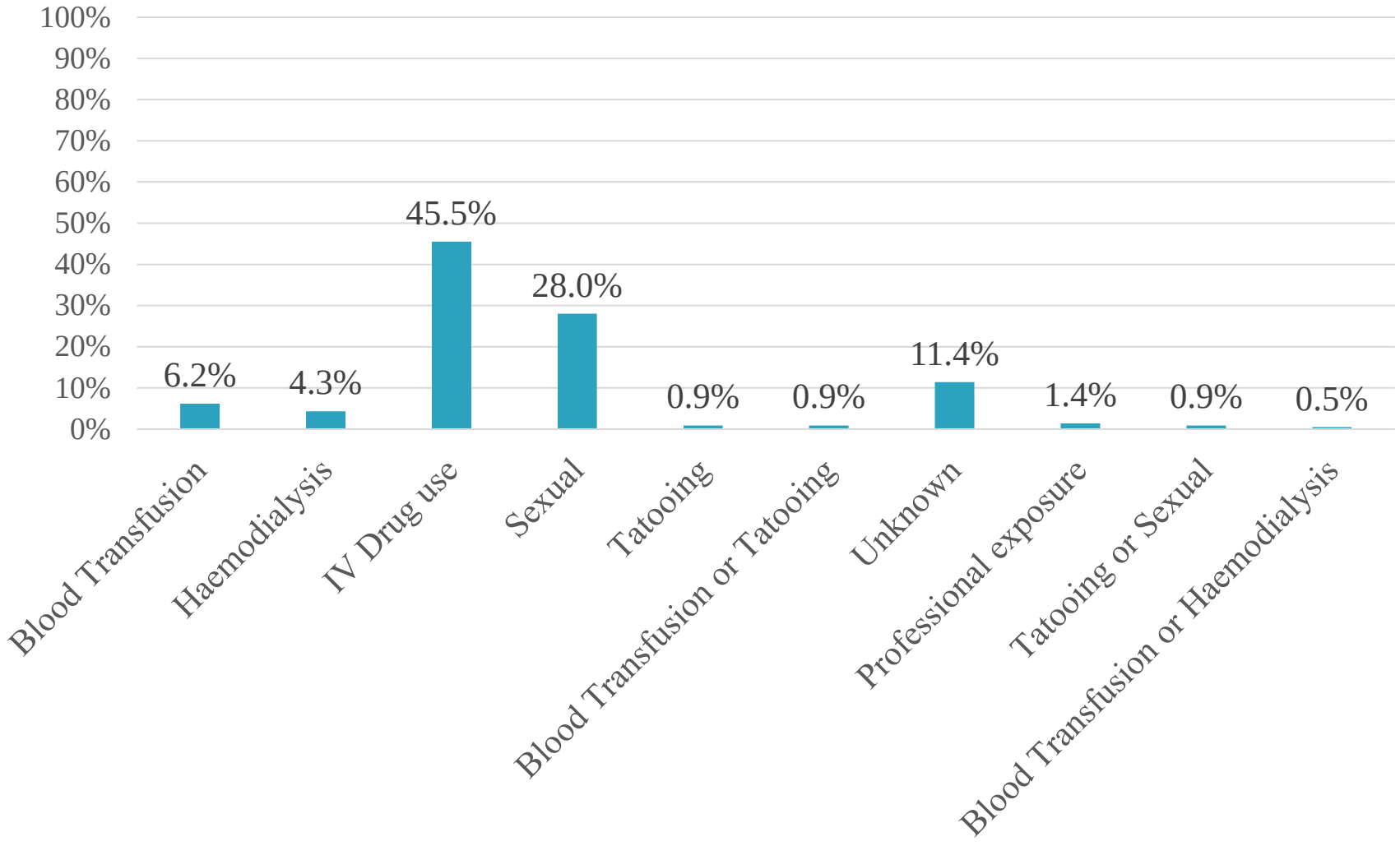
Variables		Number	Percentage
Religion	Buddhist	25	11.8
	Christian	18	8.5
	Hindu	163	**77.3**
	Islam	3	1.4
	Kirat	2	0.9
Alcohol intake habits	Regular Alcoholic	70	**33.2**
Education	Illiterate	18	8.5
	Illiterate	193	91.5



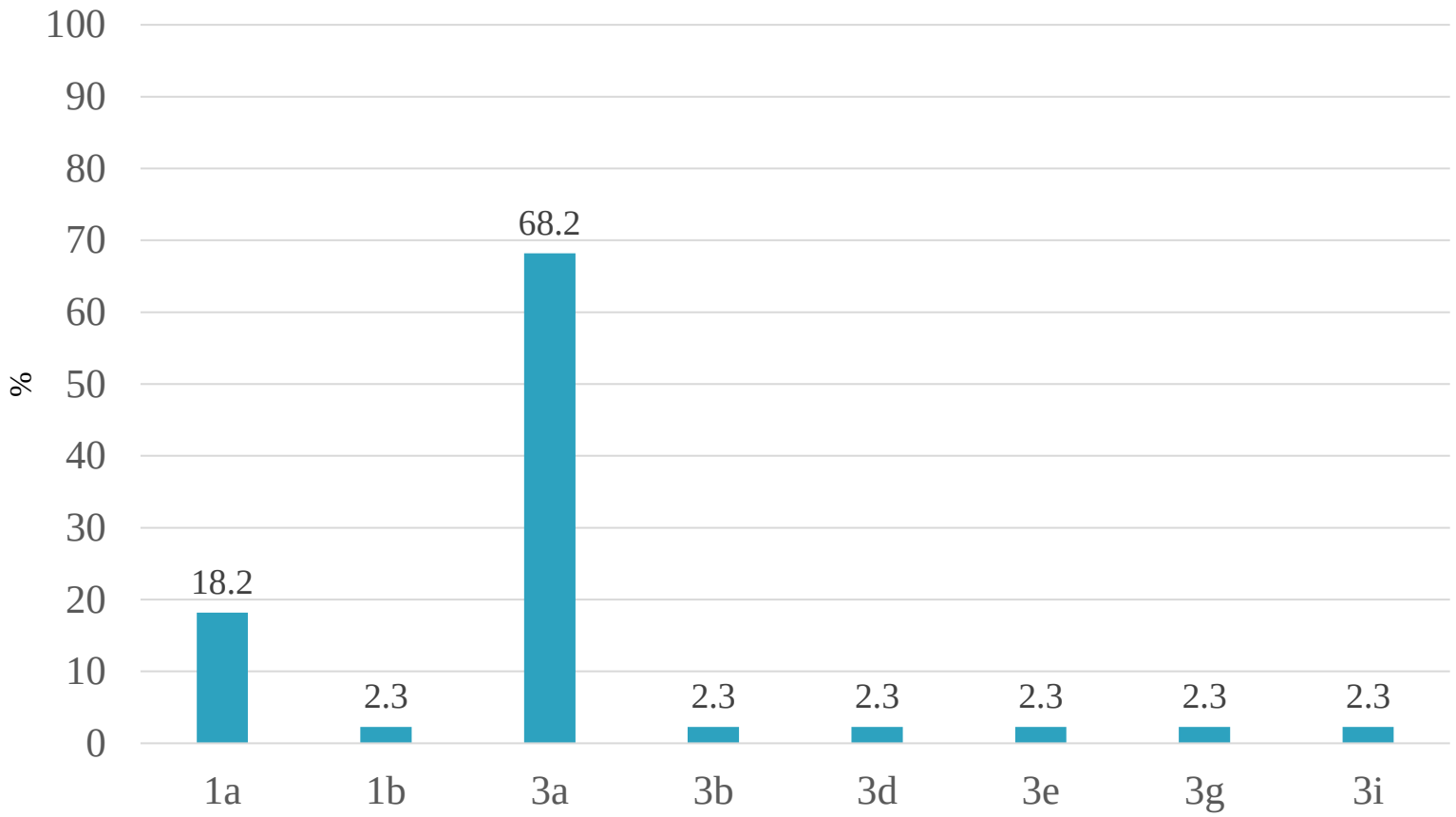
Co-infection of HCV patients with HIV& HBV(N=211)



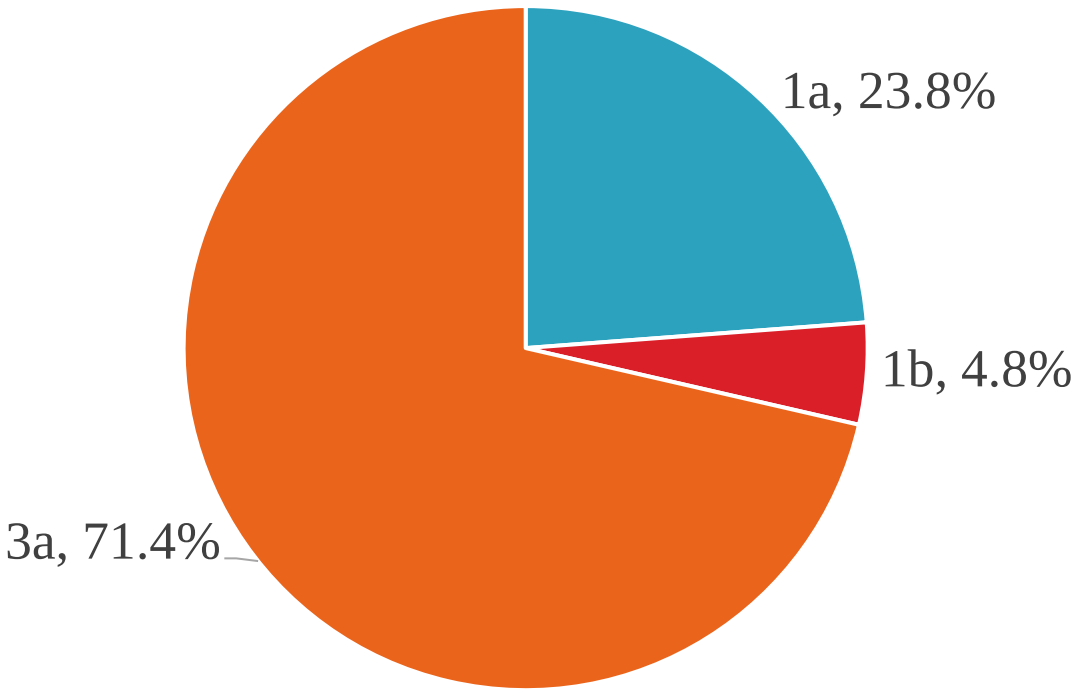
RNA positivity among HCV patients (N=211)



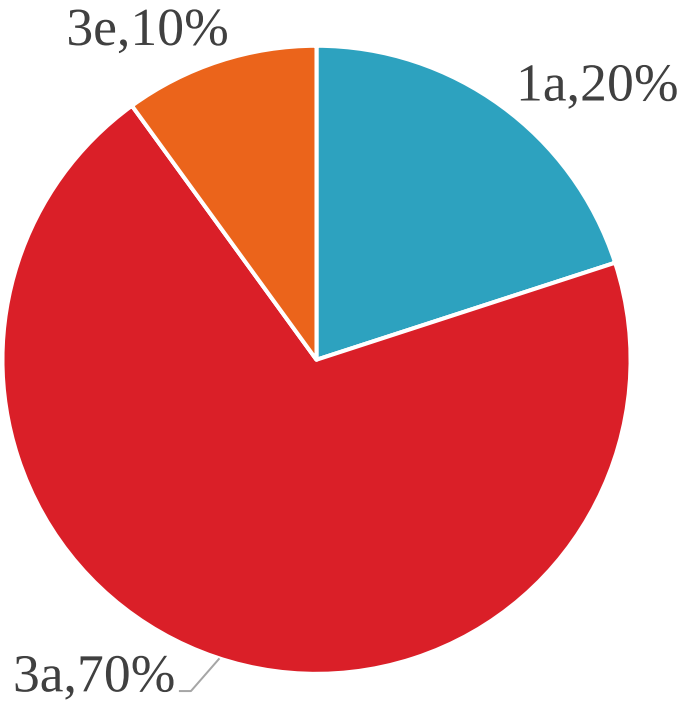
Self reported mode of transmission of HCV in Nepal(N=211)



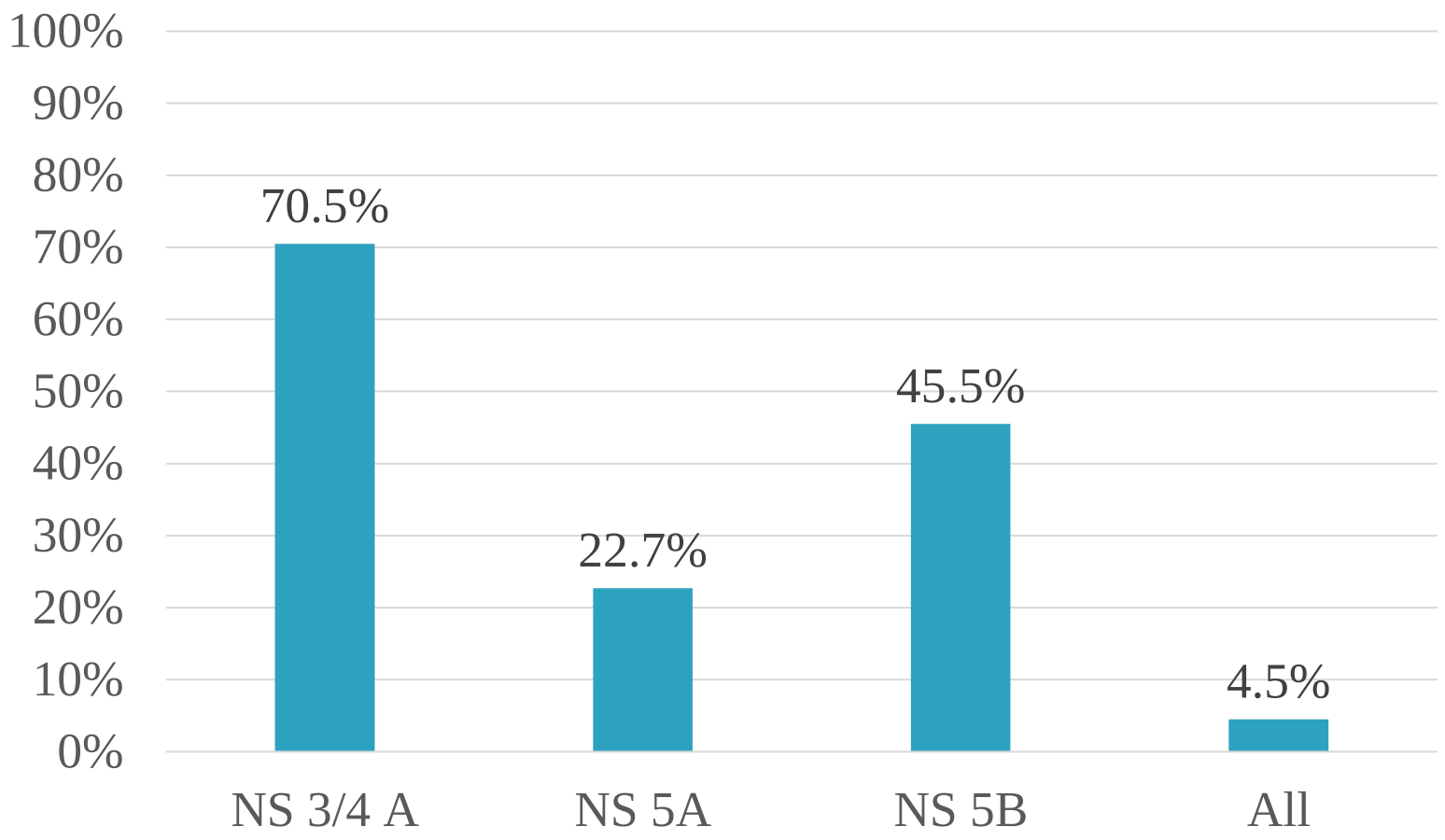
Genotype/Subtype distribution of HCV (N=44)



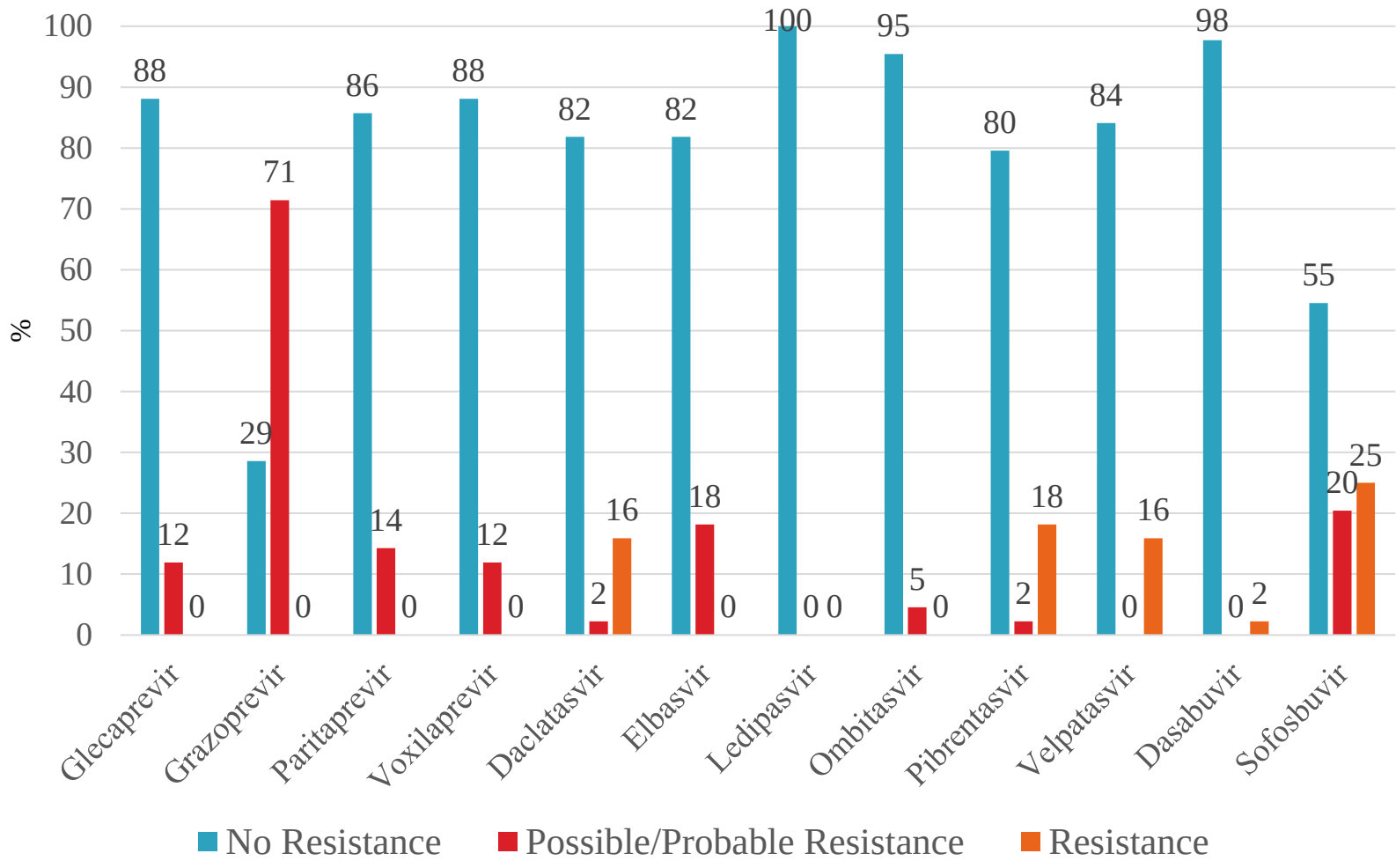
Genotype/Subtype distribution of HCV among IV drug use route of transmission (N=21)



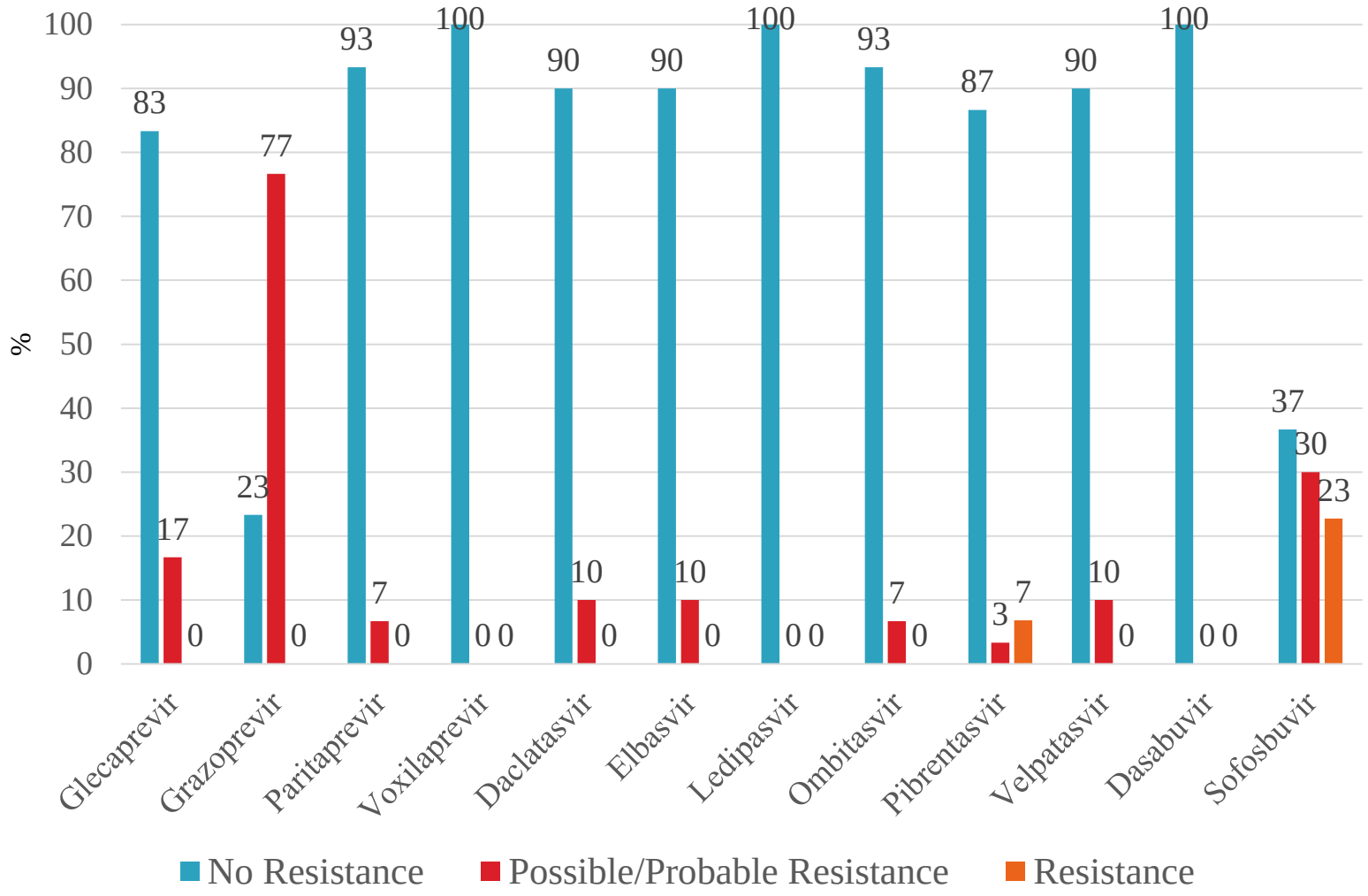
Genotype/Subtype distribution of HCV among sexual route of transmission (N=10)



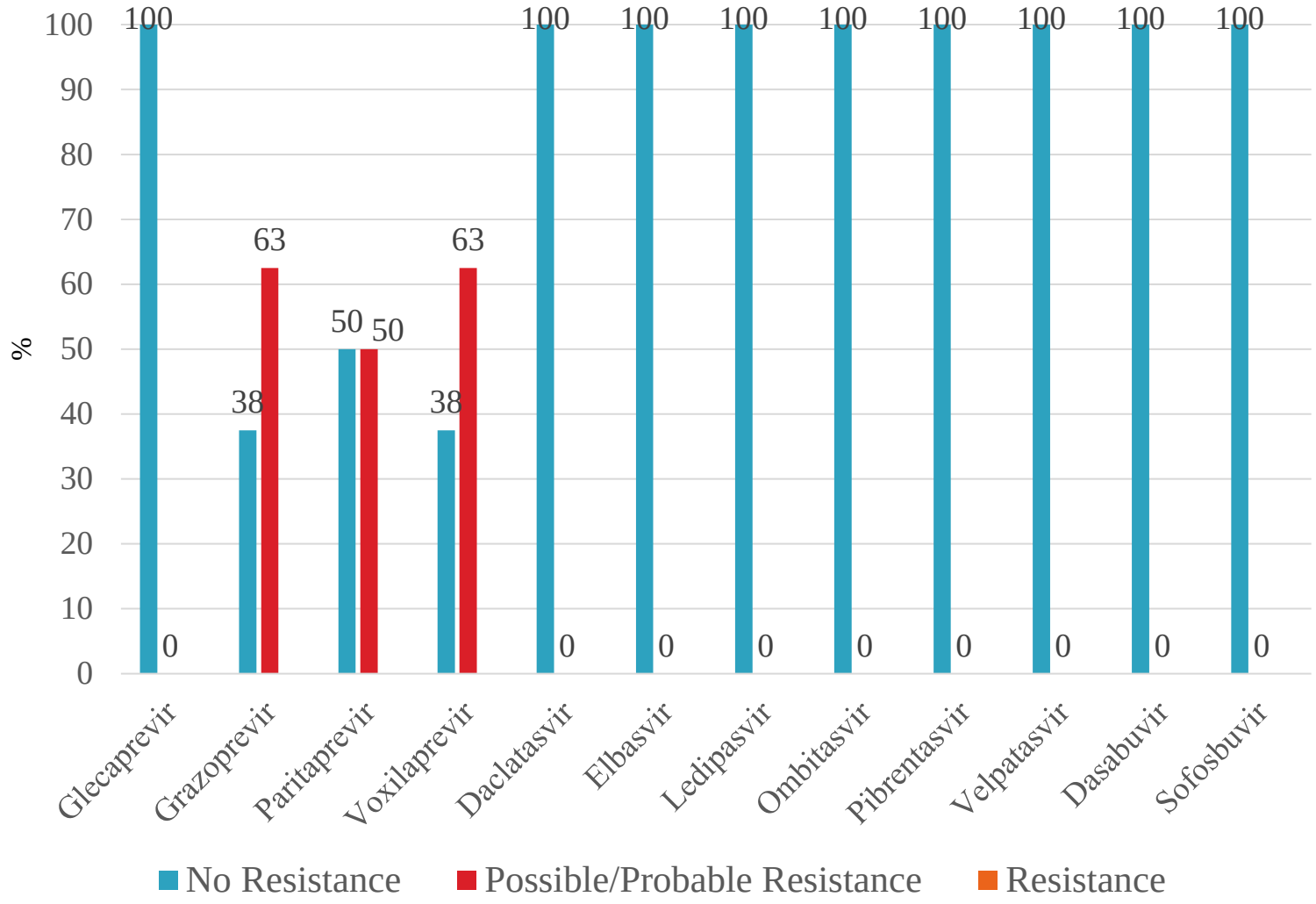
Polymorphisms and resistant mutations on DAA drugs target site of HCV genome(N=44)



Anti-viral drug profile for all genotypes(N=44)



Anti-viral drug profile for genotype 3a(N=30)



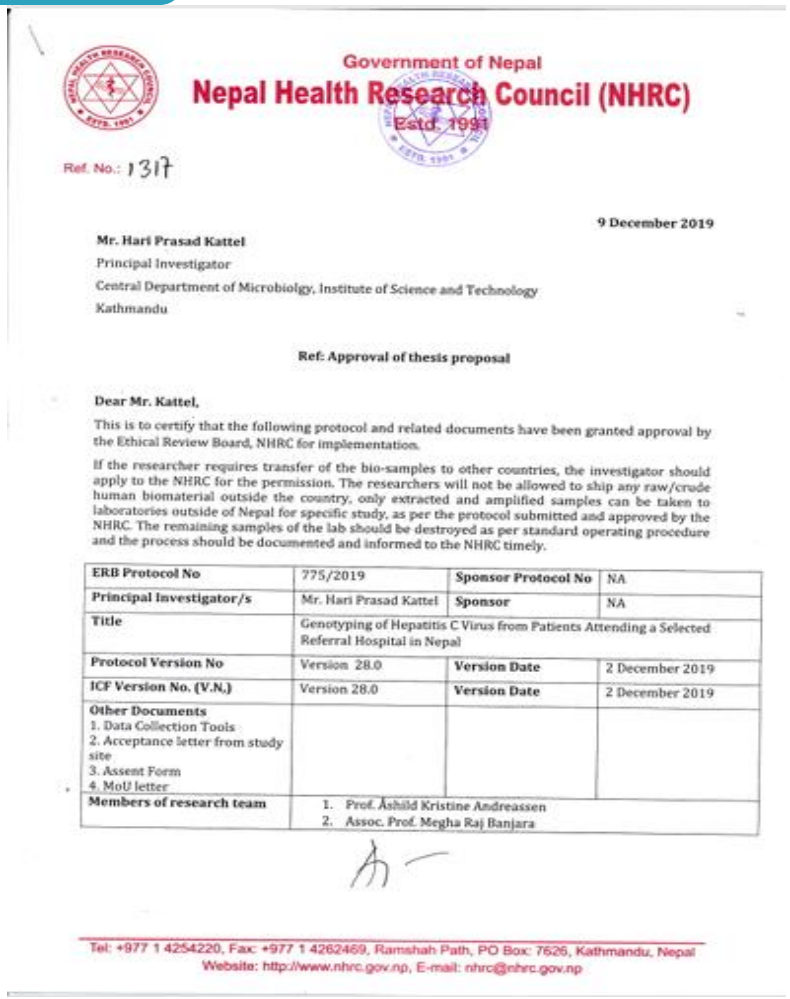
Anti-viral drug profile for genotype 1a(N=8)

Conclusions

- The predominant HCV genotype was 3 and subtype 3a
- Resistant mutations in the antiviral drug target genes were detected in the HCV genome
- HCV Genotype/subtype 3g, 3i identified from Nepal

Ethical Consideration

- Nepal Health Research Council
- Informed written consent from patients



Government of Nepal
Nepal Health Research Council (NHRC)
Estd. 1991

Ref. No.: 1317

9 December 2019

Mr. Hari Prasad Kattel
Principal Investigator
Central Department of Microbiolgy, Institute of Science and Technology
Kathmandu

Ref: Approval of thesis proposal

Dear Mr. Kattel,

This is to certify that the following protocol and related documents have been granted approval by the Ethical Review Board, NHRC for implementation.

If the researcher requires transfer of the bio-samples to other countries, the investigator should apply to the NHRC for the permission. The researchers will not be allowed to ship any raw/crude human biomaterial outside the country, only extracted and amplified samples can be taken to laboratories outside of Nepal for specific study, as per the protocol submitted and approved by the NHRC. The remaining samples of the lab should be destroyed as per standard operating procedure and the process should be documented and informed to the NHRC timely.

ERB Protocol No	775/2019	**Sponsor Protocol No**	NA
Principal Investigator/s	Mr. Hari Prasad Kattel	**Sponsor**	NA
Title	Genotyping of Hepatitis C Virus from Patients Attending a Selected Referral Hospital in Nepal		
Protocol Version No	Version 28.0	**Version Date**	2 December 2019
ICF Version No. (V.N.)	Version 28.0	**Version Date**	2 December 2019
Other Documents 1. Data Collection Tools 2. Acceptance letter from study site 3. Assent Form 4. MoU letter			
Members of research team	1. Prof. Åshild Kristine Andreassen 2. Assoc. Prof. Megha Raj Banjara		

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