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## Letter to the Editor

# Heterogeneous distribution of HCV genotypes and growing menace of mixed HCV infection in blood recipients in Khyber Pakhtunkhwa

Dear Editor,

Globally hepatitis C virus (HCV) infection touched the epidemic proportions.<sup>1</sup> In Pakistan HCV serofrequency are also significantly high.<sup>2</sup> HCV shows extreme genomic heterogeneity.<sup>3</sup> It marks an average one error per 10,000 nucleotides copied every time thus multiple strains emerged with a mutation.<sup>4</sup> These strains are genetically quite variable, make thousands of replicas (about 10 trillion particles per day)<sup>3</sup> and evade from host immune system as they are immunologically different from their ancestors.<sup>1,4</sup>

This genomic heterogeneity is a major challenge in development of effective and appropriate antiviral treatment. On the basis of similarity of nucleotide sequences HCV is classified into genotypes (65.7%–68.9%), subtypes (76.9%–80.1%), and quasispecies (76.9%–80.1%). The characterization and determination of specific molecular epidemiology is important for disease outcome, disease progression, therapeutic response, and chronicity of infection.<sup>1,5</sup>

To study the key dynamics of mixed HCV infection and to help healthcare systems to combat the burden of predominant genotypes in Khyber Pakhtunkhwa (KPK), Pakistan. 4607 individuals with age range of 1–75 years were investigated. Anti-HCV positivity was reported in 17.39% individuals and HCV RNA was diagnosed in 8%. HCV genotypes were determined in 72.5% individuals while 0.69% individual's genotypes were not defined by the prescribed system. Genotype 1 was accounted for 20.9% of individuals and subtype 1a predominated (6.49%), followed by 1b (4.12%) and 1c (1.03%). Genotype 2 was found in 5.01% and subtypes were reported as 2a (3.24%), 2b (1.45%), and 2c (0.29%). Genotype 3 alone was reported in 53.69% and subtypes were reported as 3a (38.64%), 3b (11.21%) and 3c (3.83%). Genotype 4 frequency was 4.72% and subtypes were 4a (2.95%), 4b (1.77%). Subtype 5a and 6a accounted for 4.72% and 3.54% individuals, respectively. This study reported that among mixed genotypes, 3a alone or in combination with other types was more prevalent, in accordance with previously published results that 3a is the major HCV genotype circulating in KPK with a prevalence of 45.5%.<sup>2</sup> High prevalence

of genotype 3 is a good sign as it needs shorter duration of treatment when compared to genotype 1.<sup>5</sup>

In this study mixed genotype was reported in 7.37% individuals as 3a+3b (3.54%), 3a+3c (2.94%), 2a+2b (2.94%), 3a+1b (1.77%), and 3a+1a (1.47%). A high proportion of genotype 3a+3b in this study agreed with the study of Butt et al. (43.79%),<sup>6</sup> in contrast to another study that 3a+1b was most prevalent (49%) followed by 3a+3b and 1a+1b with rates of 15% and 15%, respectively.<sup>2</sup> Literature reported that in Pakistan mixed HCV genotype pattern are similar to the neighboring nations.<sup>5,6</sup> Moreover immigrants from these countries bearing high HCV load is responsible for the influx of new and hybrid strains and modifying epidemiological data.<sup>2,5</sup>

It was noteworthy that 1.2% mixed genotype (3a+3b and 2a+2b) was found in thalassemia patients, 1.5% (3a+3b, 1b+3a and 3a+3c) in hemodialysis patients, 3% (3a+3b, 1b+3a and 1a+3a) in hemophilia patients, and 0.6% (3a+1b and 1a+3a) in surgical patients. Statistical significance was reported for HCV infection between surgical patients and hemophilia patients ( $\chi^2=74.896$ ,  $p<0.0001$ ), thalassemia patients and surgical patients ( $\chi^2=35.79$ ,  $p<0.0001$ ), thalassemia patients and hemodialysis patients ( $\chi^2=6.158$ ,  $p=0.013082$ ), thalassemia patients and hemophilia patients ( $\chi^2=12.28$ ,  $p<0.0001$ ) and surgical patients and hemodialysis patients, ( $\chi^2=162.3$ ,  $p<0.00001$ ). However, the difference between hemodialysis patients and hemophilia patients ( $\chi^2=0.1192$ ,  $p=0.73$ ) was not statistically significant. These findings showed that mixed HCV genotypes infections were associated with high levels of exposure to blood transfusion in this study. The aforementioned risk group has been poorly addressed in the past literature of our country. Till now no large study had documented the HCV genotypes in these vulnerable populations. These findings highlighted that unsafe blood transfusion is one of the main obstacles for HCV control in our community which strongly emphasizes on the need to restrain HCV transmission to the least level through blood transfusion in the country by gagging blood safety filters in place.

In conclusion, mixed genotype HCV infection has penetrated the KPK population, especially through unsafe blood transfusion. Mixed molecular epidemiology is essential to depict accurate figures in different populations so to track and minimize their route of transmission to the least level.

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### Authors' contributions

SK and SA designed, analyzed the data and prepared the manuscript. SA collected the data and samples and performed experimental work. MZ gave critical review of manuscript writing. All the authors read and approved the final manuscript.

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### Conflicts of interest

The authors declare no conflicts of interest.

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