



Prevalence of Genotype 3a in Different Regions of Pakistan: A systematic Review and Meta-Analysis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i44A32628

Editor(s):

(1) Dr. P. Veera Muthumari, V.V. Vanniaperumal College for Women, India.

Reviewers:

(1) J. Venkateshwara Rao, Osmania University, India.

(2) Mohammad Daud Ali, Mohammed Al-Mana College for Medical Sciences, Saudi Arabia.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/73157>

Systematic Review Article

Received 05 July 2021

Accepted 15 September 2021

Published 20 September 2021

ABSTRACT

The present study aims to explore the prevalence of genotype 3a under hepatitis C virus (HCV) infections among all the provinces of Pakistan. It is alarming to note that Pakistan stands in the second position for having a large number of cases of HCV every year. Six major genotypes characterize HCV. To study the overall prevalence of HCV and its associated genotype 3a in all the provinces of Pakistan, a systematic review and meta-analysis were performed using STATA version 14.2. The published studies conducted in all the regions of Pakistan reported the incidence of HCV genotype 3a were shortlisted. The pooled summary estimates were calculated along with their confidence interval by using the "Metaprop" command. The literature review showed that the prevalence of HCV genotype 3a is most common in all the provinces of Pakistan. It is revealed that the prevalence of HCV genotype 3a was 86.46% in Punjab, which is the highest among all the regions.

Keywords: HCV; genotype3a; prevalence; meta-analysis; systematic review.

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1. INTRODUCTION

Hepatitis C virus (HCV) is a worldwide medical problem influencing approximately 3% of people worldwide [1]. About 71 million people are suffering from the disease's chronic stage, resulting in a high risk of liver cancer or liver cirrhosis [2,3]. The deadly disease leads to individual liver problems, around 350,000 individuals' yearly loss of their lives around the globe [4]. There are various treatments to cure hepatitis, out of which antiviral medicine can treat 95% of the patients successfully [5,6].

Based on the variation in sequencing the virus, there are six genotypes of HCV and many subtypes [7,8]. Genotype 1a and 1b are prevalent in Europe and United States whereas, genotype 2 is more influential in West Africa [9]. South Africa and Australia are more infected regions in terms of genotype 3's prevalence [10]. In Central Africa and Egypt, the most prevalent type of HCV virus is genotype 4 [11,12]. In Addition to this, genotype 5 and 6 are found to be more commonplace in South Africa and Asia [4]. Globally, genotypes 1 and 3 are the most common types [10]. Whereas genotypes 4 and 5 are more prevalent in lower-pay nations.

HCV has become a prominent health issue worldwide with severe consequences related to liver disorders. It has been reported that transference of HCV can be due to dental services, shaving, sexual contact, and IV drugs. Untrained medical staff also plays a significant role in HCV transference for specifically genotype 3 ($p < 0.05$) [13].

In Pakistan, 6% of the population is infected with HCV [14]. A flawed healthcare system, untrained medical staff, non-sterilized syringes, poverty, and lack of awareness are some of the common factors through which HCV is transmitted [15]. Concerning the different genotypes, the prevalence of HCV in Pakistan varies across its provinces [16]. Several studies have suggested that the most prevalent genotype of the Hepatitis C virus in Pakistan is genotype 3a [17-21]. The prevalence of genotype 3a is 86.46% in Punjab, which is the highest among all regions of Pakistan, it is found to be 61% in Sindh and 50% in Balochistan [14]. As per the studies conducted in Pakistan, genotype 2a is rising in KPK, rare in other provinces [22,23]. It is of prime importance to note that, in FATA, the prevalence of HCV is 0.9% [15,24].

2. METHODOLOGY

2.1 Literature Search

A systematic review and meta-analysis require many already published studies relevant to the topic of the study. So, periodic review begins with a deep and extensive search of collecting such articles. Several available online databases, such as Google Scholar, PubMed, Jstor, Elsevier, etc., were accessed to gather the studies. Only those studies were shortlisted which reported the genotype 3a of HCV in Pakistan. All the collected articles were from authentic and indexed journals, and their medium was English.

2.2 Criteria for Inclusion and Exclusion of Articles

Meta-analysis is dependent on collecting the relevant studies. Still, it is also essential to finalize these articles or studies after properly assuring their quality and critically analyzing whether they meet the selection criteria. The inclusion and exclusion criterion used in our research is as follows:

- i. Only the researches having full-text content were included.
- ii. The studies that reported the concerning variables, like the prevalence of genotype 3a, were part of the systematic review.
- iii. The articles having low-quality study patterns were not included in the analysis.
- iv. The studies not having the data on variables of interest were also excluded.

2.3 Data Extraction

After the extensive search and gathering of the relevant studies, the next step is to obtain the data. This step requires care and vigilance as it sets the foundation of the analysis. Data on the prevalence of HCV genotype 3a was recorded for different regions (provinces of Pakistan). Data obtained from the finalized articles was fed into an excel sheet that was then imported to SPSS. These files were later changed to the format of STATA (version 14.2) to be used for necessary analysis.

2.4 Statistical Analysis

Before the selection of the model, it is of prime importance to set an appropriate effect size. The function of effect size is to standardize the differences present between the studies. The proportion was used as the measure of effect

size in this research. Meta-analysis mainly takes up two types of models to produce pooled estimates. These models are termed "Fixed-effect" and "Random-effect" models. The choice of the model depends upon the structure of the data on which we wish to carry out a meta-analysis. The weight assigned to each study is determined by the type of model being used in the meta-analysis. The "Fixed-effect" model does not consider the variation between the studies, whereas the "Random-effect" model is based on the fact that both variations within and between studies are considered. For achieving our desired objective of computing the pooled estimates of the proportion of HCV genotype 3a in each province of Pakistan, the "Fixed-effect" model was chosen. "Metaprop" command, found in STATA (version 14.2), was used to carry out a meta-analysis for proportion [25]. The key characteristics of the fixed-effect model are as follows:

- The fixed-effect model is suitable for research belonging to the same population, implying that all the finalized research must have the same underlying methodology. Also, this model assumes a constant population effect size for all the studies.
- The fixed-effect model requires such studies in which one-level sampling is done, which implies that only one source of error is present in the research included in the meta-analysis. This source of error might be due to sampling methods or other human errors, and these sampling errors are the reason for

the differences between the observed effect-sizes. The weight of each study is the inverse of the error variance. So, if 'Z' is the error variance, then '1/Z' would be the weight for each study.

- The fixed-effect model only deals with the variation within the studies.
- Fixed-effect is of the following form: " $U_j = \theta + e_j$ " where " U_j " is the observed effect size, whereas θ represents the population effect size. The sampling variance of U_j is represented by $\text{var}(e_j)$. Independence among the studies is assumed.
- Pooled effect-size in the fixed-effect model is computed using the following formula:

$$\bar{U} = \frac{\sum_{j=1}^n w_j U_j}{\sum_{j=1}^n w_j}$$

Where 'n' is the number of studies, $w_j = 1/Z_j$ is the weight.

- Sampling variance of \bar{U} is given by:

$$S^2 = \frac{1}{\sum_{j=1}^n w_j}$$

3. RESULTS

The results of the Meta-Analysis using the fixed-effect random approach for each province of Pakistan are pasted below.

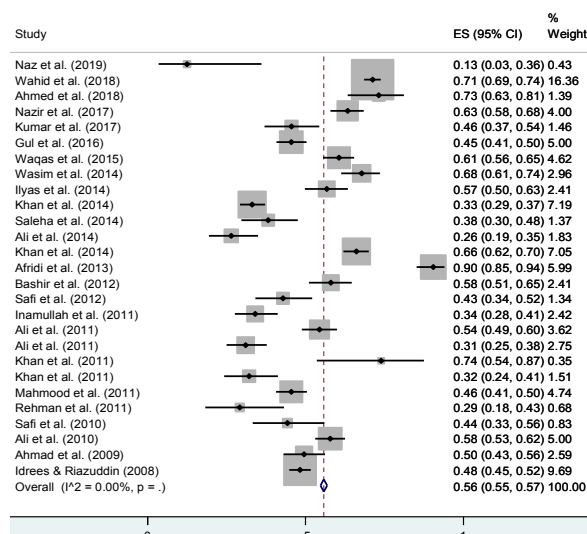


Fig. 1. Forest plot for the individuals diagnosed with genotype 3a of HCV in KPK

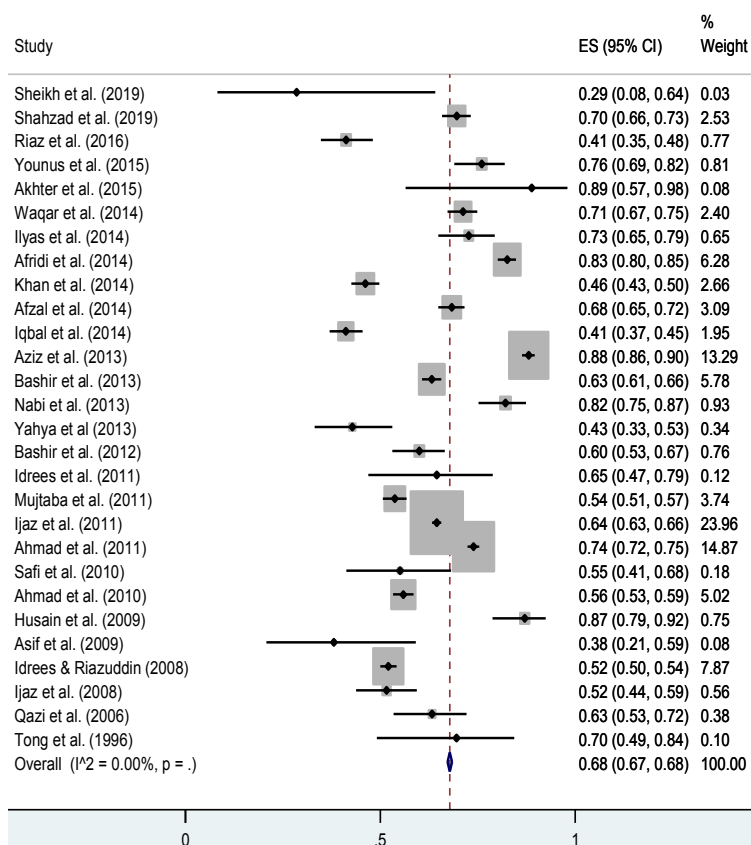


Fig. 2. Forest plot for the individuals diagnosed with genotype 3a of HCV in Punjab

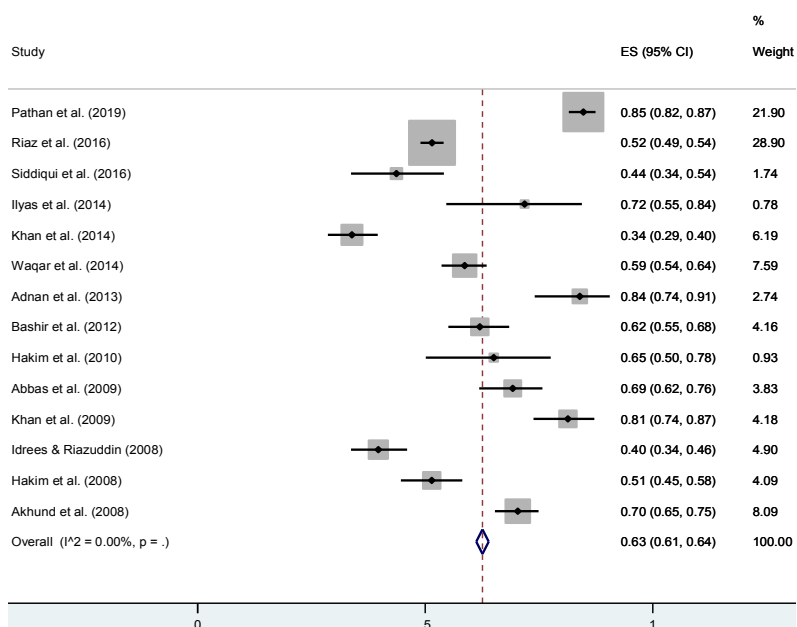


Fig. 3. Forest plot for the individuals diagnosed with genotype 3a of HCV in Sindh

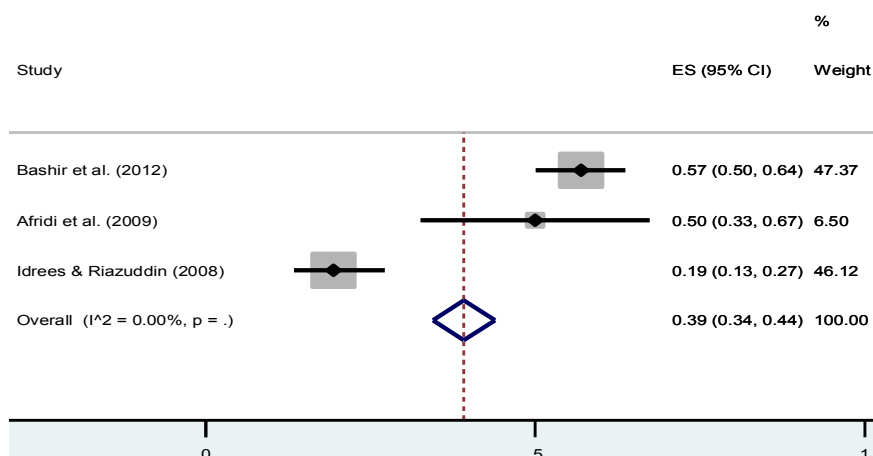


Fig. 4. Forest plot for the individuals diagnosed with genotype 3a of HCV in Balochistan

4. DISCUSSION

"Hepatitis C virus (HCV)" has been a challenge for Asian Countries for decades now. Therefore, it requires an in-depth analysis of its associated genotypes. There are majorly six genotypes and 67 subtypes. Several routes have been identified through which HCV can be transmitted. Out of which, the poor healthcare system, lack of awareness, untrained medical staff, reuse of syringe, sexual contact are more significant factors. This life-threatening disease can lead an individual to other poor health conditions out of which the liver gets affected the most. Liver inflammation, Liver cancer, liver cirrhosis are some of the problems that occur due to HCV. Developing and developed countries face this infectious disease as per the statistics reported by WHO in 2015, there were 1.75 million new HCV cases. According to the graphical distribution of Pakistan, the most common genotype of HCV in Pakistan is genotype 3a is more prevalent in all the provinces of Pakistan. Punjab, being the most populated province, has the highest prevalence of HCV i.e., 86.46%.

The operational procedure of Meta-Analysis requires a vast literature search. By exploring different search engines, 101 articles were collected based on relevancy. After going through the research articles, 26 were shortlisted and included in the analysis. The meta-analysis results revealed that the pooled estimate for the prevalence of HCV genotype 3a in KPK is 0.56, implying that 56% of its population is infected with HCV genotype 3a. For the summary estimate, the confidence interval ranged between 0.55-0.57. The highest pooled prevalence of

HCV genotype 3a was seen in Punjab, 68%, with the confidence interval 0.67-0.68. In Sindh, HCV genotype 3a accounts for 63% pooled prevalence, with 0.61-0.64 being the range of the respective confidence interval. Balochistan has the lowest pooled prevalence of genotype 3a, equal to 39%, with a confidence interval of 0.34-0.44.

With the growing population, HCV is also becoming more prevalent, which is evident from the analysis suggesting that the most populated province of Pakistan has the highest percentage of HCV prevalence. To minimize the outrageous impact of this disease, awareness campaigns must be carried out to educate the people. Moreover, many preventive measures are required in the healthcare systems to prevent this fatal disease.

5. CONCLUSION

The present research was conducted to highlight the prevalence of HCV genotype 3a in Pakistan. To find out the trend of HCV genotype 3a, a detailed systematic review was carried out. Moreover, Meta-Analysis using STATA version 14.2 was performed, and summary estimates were calculated. Based on the obtained results, it is concluded that compared to the other provinces of Pakistan, Punjab has a substantial prevalence of HCV genotype 3a, which came out to be 68%. At the same time, the lowest pooled prevalence was found in Balochistan. To control the prevalence of this deadly disease, the hour needs to spread proper awareness. Furthermore, the betterment of the healthcare system is equally essential in minimizing the rate of HCV.

DISCLAIMER

The products used for this research are commonly and predominantly used in our research area and country. There is no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for litigation but the advancement of knowledge. Also, the research was not funded by the producing company.

CONTENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENT

The current research is a part of a funded research project awarded by the University of the Punjab Lahore, Pakistan (2020). Therefore, the authors are thankful to the project awarding institution.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:

*The peer review history for this paper can be accessed here:
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