A Dire Need To Break The Back Of Hepatitis C Virus In KP-Pakistan: A Meta-Analysis

Ali Zalan[1], Iftikhar ud Din[2], Dr. Najeeb Ullah Khan[1], Saqib Elahi[1]

[1]Institute of Biotechnology & Genetic Engineering (IBGE), The University of Agriculture Peshawar
[2]Department of Maths, Stats & Computer Science, The University of Agriculture Peshawar

Corresponding Authors' email: alizalan1997@gmail.com, Iftikhar.din1@gmail.com, najeebkhan@aup.edu.pk, saqibelahi69@gmail.com

ABSTRACT

Viral Hepatitis is the seventh leading cause of death worldwide and prevails in many developing countries specifically in the Middle East and North African regions. The current study focuses on a comparatively low-income province of Pakistan, Khyber Pakhtunkhwa where medical facilities are scarce and the use of blood and its products, free from viral hepatitis and other pathogens, is poorly ensured. The preliminary phase of the study involved a systematic literature review on the epidemiology of Hepatitis C Virus in KP during the period 2000-2018 through PubMed, Science Direct, and Google Scholar. After statistical coding, an initial meta-analysis was conducted to come up with an integrated estimate of the prevalence of Hepatitis C Virus in Khyber Pakhtunkhwa. The prevalence rate of 4% by fixed effect model and of 6% by random effect model is extremely alarming, especially in a low-income region, and the Pakistani government should adopt effective and rapid strategies to eliminate Hepatitis C Virus infection by the end of 2030, as more times announced by the World Health Organization.

Keywords: Hepatitis C virus, Meta-Analysis, Khyber Pakhtunkhwa-Pakistan

Background

Viral hepatitis is the main cause of liver cirrhosis, fibrosis, and cancer and is estimated to cause around 700 000 deaths each year. [1,2]. Hepatitis C Virus (HCV) belongs to the Flaviviridae family, which covers a huge group of viruses that are enveloped and have a single-strand RNA genome of positive polarity [3]. Direct-acting antivirals (DAAs) is an extremely effective HCV treatment that can clear HCV infection and lessen HCV disease burden and further transmission [4]. World Health Organization (WHO) has set global targets to eliminate HCV infection by 2030. [5]. HCV is the principal cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC). Chronic HCV infection is reckoned to infect 130 to 150 million globally (with an estimate of 55%-85% cases progressing to chronic liver disease, 15%-30% cases progressing to cirrhosis and 1%-5% are expected to die due to decompensated cirrhosis and HCC [6-9]. Globally, 80% of the HCV burden is concentrated in low and middle-income countries (LMICs) [10]. The prevalence varies by region and can be concentrated in a certain type of population e.g., in people who inject drugs (PWID) in which the prevalence can reach up to 67.1% [11]. The prevalence of HCV differs worldwide, but the highest incidence rates are reported in the Middle East and North African regions (MENA countries) and also in some European countries belonging to the Mediterranean area [12-13]. HCV is widespread in many MENA countries where Egypt shows the highest rate of HCV (estimated at >10%) [14]. HCV infection is massively endemic in Pakistan, with an estimated prevalence of 4.54-8,2%, second only to Egypt. Out of the six major HCV genotypes, the genotype 3a is predominant (69.1%), followed by genotypes 1 (7.1%), 2 (4.2%), and 4 (2.2%) [15]. In Pakistan, HCV transmission is mainly driven by multiple risk factors, such as health care practices, community-based activities (barbering, ear/nose piercing), and injecting drug use [15- 16]. Thus, it is important to investigate the epidemiology of HCV to plan appropriate strategies for detection, treatment, and prognosis. This study aims to determine the incidence of HCV in KP-Pakistan, through an analysis of already published data from 2000–2020 using R- statistical software. Understanding HCV

epidemiology in Pakistan is crucial not only in terms of prevention and treatment but mainly for the global purpose of HCV eradication.

Main text

This study was conducted following e PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [17].

Data Source and Search Strategy

The searches were conducted using Google Scholar, PubMed, Science Direct, WHO database, and publications of Health Department KP to identify all the articles reporting the epidemiology of HCV in KP. Information was collected from these databases from 2000 to January 14th, 2018. An extensive search criterion was used with no language constraints. The keywords used were: [Hepatitis C in Pakistan, Hepatitis C in Khyber Pakhtunkhwa, Hepatitis C in Northwest Frontier Province (previous name of KP), Hepatitis C in NWFP, Prevalence of HCV in KP, and Epidemiology of HCV in KP-Pakistan].

Study Inclusion Criteria

The study period (2000-2018) was focused on the epidemiology of HCV over the last two decades or from the beginning of the 21st century. All records identified (n=80) were imported into Mendeley, a reference manager, where duplicate publications were identified and excluded (n=13). The studies had

to meet the criteria for selection: clearly stated objective, clearly described study design, type of population (e.g., General, PWIDs, Blood donors), adequate sample size, and diagnosis method. Further descriptive information such as

reported HCV prevalence, the region of KP, author details, and publication year were collected. There were no age restrictions. After performing primary and secondary selection, 41 studies were included in the study as shown (Figure

Figure 1: Flow chart of article selection as adapted by PRISMA
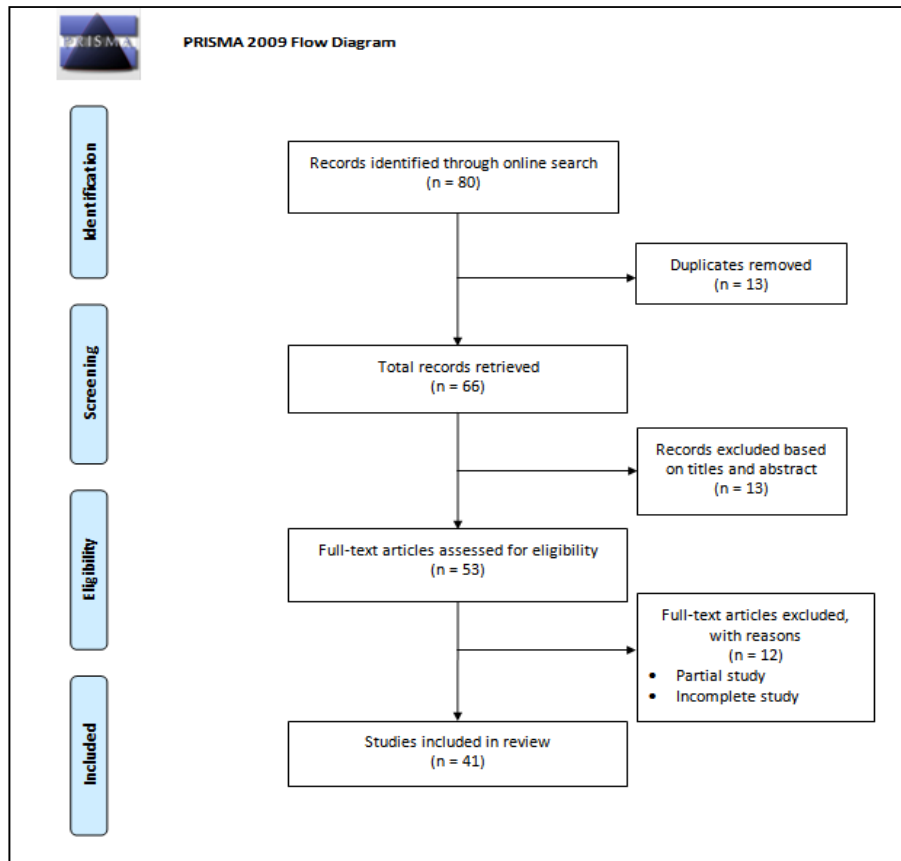
Data Analysis

A total of 41 eligible studies with a cumulative sample size of 316,061 were included and analyzed. Further, the studies were ranked according to their scores into high, medium, or low, relating to HCV incidence. Out of 41, 27 studies represented the general population, and 14 were with high-risk populations. After statistical coding, an initial meta-analysis was conducted to come up with an integrated estimate of the prevalence of HCV in KP. These estimates were found for the fixed effect and the random effect model. To assess the sample heterogeneity Q statistics were calculated. Although Cochran's Q is commonly reported, I^2

has been recommended as a supplement to Q when assessing heterogeneity because, unlike Q, I^2 allows researchers to quantify heterogeneity and to compare the degree of heterogeneity within different analyses [18,19]. Thus, an I^2 value of 25% indicates that one-quarter of the variation between studies reflects systematic or heterogeneous variation, rather than random sampling error.

The forest plot, useful tool of meta-analysis, was constructed to give a better picture of the prevalence from individual studies and the divergence from the overall combined estimate, 95% confidence interval, and weights were assigned to each study by the fixed effect and random effect model. Further, to highlight the

amount of publication bias, funnel plots and regression tests were incorporated. The above process was repeated to compare the gender-wise prevalence of HCV. Out of 41, 26 studies that reported HCV in male and female populations were statistically analyzed, and an odds ratio was used to compare the prevalence of HCV in male and female populations. Further details were found using the Forest plot, funnel plot, and regression test. Although meta-analysis is a useful tool for integrating research findings, one of its major advantages is that it allows an examination of the extent to which findings are due to either random sampling error or systematic variations (heterogeneity) between studies. We conducted a meta-analysis by R (version 3.3.3), a language and software environment for statistical computing [20,21].

Study Characteristics

Extracted data is graded by study populations' risk of HCV infection in two groups as shown (Table 1 and 2), General Populations and High-Risk Populations.

1. In group 1, eleven studies present general group (Table 1), seven studies present the population of blood donors, five studies report the prevalence of HCV in pregnant women, two studies report the epidemiology of HCV in Health Care Workers, one study reports the epidemiology of HCV in Civil Servants and one study reports the epidemiology of HCV in Internally Displaced People (IDPs).

2. In group 2, fourteen studies present different types of the population at high risk including patients admitted in hospitals, Cataract Patients, Clinically suspected cases of HCV, Dental Patients, Gynecological patients, Hemophilia patients, Liver disease patients, Orthopedic patients, High-risk groups, and Thalassemia Patients.

The serological methods reported in studies of both the groups were CMIA, ELISA, ICT, IMX, and PCR.

Pooled mean HCV prevalence estimates in KP

The combined weighted estimate of HCV prevalence in KP, obtained from 41 previously conducted studies is 4% using the fixed-effect model and 6% from the random effect model (Figure 2). Further, the division of these studies in general and high-risk population gives respectively 3% and 8% prevalence of HCV by fixed effect model and 4% and 11% by random effect model, while between-group comparison is highly significant (p-value < 0.0001). The significant Q statistics indicate the presence of heterogeneity among the estimate from individual studies while the associated I^2 statistics show that most of the variation between samples is systematic in both groups. These points indicate the existence of substantial moderators (Risk factors) and their relationship with HCV prevalence.

It is observed in the Forest Plot (Figure 2) that out of 27 estimates of the general population mostly larger weight studies possess low or average prevalence and are closing to the central line (combined estimate of fixed effect and random effect model). A study of blood donors carries a maximum sample size of 127,828 and consequently, possesses the largest weight in the fixed effect method (32.9%). The high-risk population studies consist of 25,944 individuals and carry a maximum weight of 8.7%. In the random effect method, the weights are only fractionally varying among the available studies. I^2 statistics and tau^2 statistics indicate highly significant heterogeneity among HCV estimates found in the individual studies. The prevalence of HCV ranges from 1% to 22% in group 1 while in group 2 it varies from 3% to 53%.

Table 1: Descriptive characteristics of studies reporting HCV prevalence in the general population of KP

GENERAL POPULATION	Sample size	Male	Fe male	HCV%	Male (+)	Female (+)	Region	Methods	Reference
General	16,40 0			4.57 %	409	342	Bune r	ELISA	[22]
	8,439			0.50 %			KPK	ELISA	[23]
	4,680	2,87 0	1,81 0	13.8 0%	252	393	Swat	ELISA	[24]
	1,978	809	1,16 9	7.90 %	74	84	Pesh awar	PCR	[25]
	1,431	308	109 3	1.47 %	12	9	Mala kand	ICT/ ELISA/ q-PCR	[26]
	1,419	757	662	8.52 %	87	34	Mard an	ICT	[27]
	982	543	439	12.9 3%	84	43	Pesh awar	CMIA	[28]
	648	254	394	10.3 0%	30	37	Man sehra	ICT	[29]
	400	300	100	7%	12	2	Man sehra	ICT	[30]
	340			17.3			Pesh	ELISA	

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			4%			awar		[31]
	180		**5%**	7	2	Peshawar	ELISA/ ICT	[32]
Blood Donors	127,828	127,780	48	**2.46 %**	3145	0	Peshawar	ELISA	[33]
	41,613	41,613		**2.23 %**	938		Swat	EIA	[34]
	32,042	32,042	0	**1.97 %**	632	0	Peshawar	ELISA	[35]
	7,148			**3.13 %**			Peshawar	ICT/ ELISA/ RT-PCR	[36]
	5,318			**2.95 %**			Mardan	ICT	[37]
	4,000	3,953	47	**2.20 %**	88	0	KPK	IMX or Axsym	[38]
	356	356		**22.20%**	79		Quetta	ICT	[39]
	10,288	0	10,288	**1.42 %**	0	146	Peshawar	ICT	[40]

High-risk population	Sample size	Male	Female	HCV%	Male (+)	Female (+)	Region	Methods	Reference
Pregnant Women									
	5,607		5,607	**2.60%**		146	Swat	ICT	[41]
	2,050		2,050	**5%**		103	Peshawar	ICT	[42]
	500		500	**8.60%**		43	Hazara	ELISA	[43]
	360		360	**2.22%**		8	Haripur	ICT	[44]
Health Care Workers	824	493	331	**4.10%**	21	13	KPK	ICT/PCR	[45]
	125	83	42	**2.40%**	2	1	Abbottabad	ELISA	[46]
Recruited Civil Servants	4,639	3,605	1,034	**3.98%**	158	27	KPK	ELISA/ICT	[47]
IDPs	590	290	300	**4.20%**	8	17	Swat	ICT/PCR	[48]

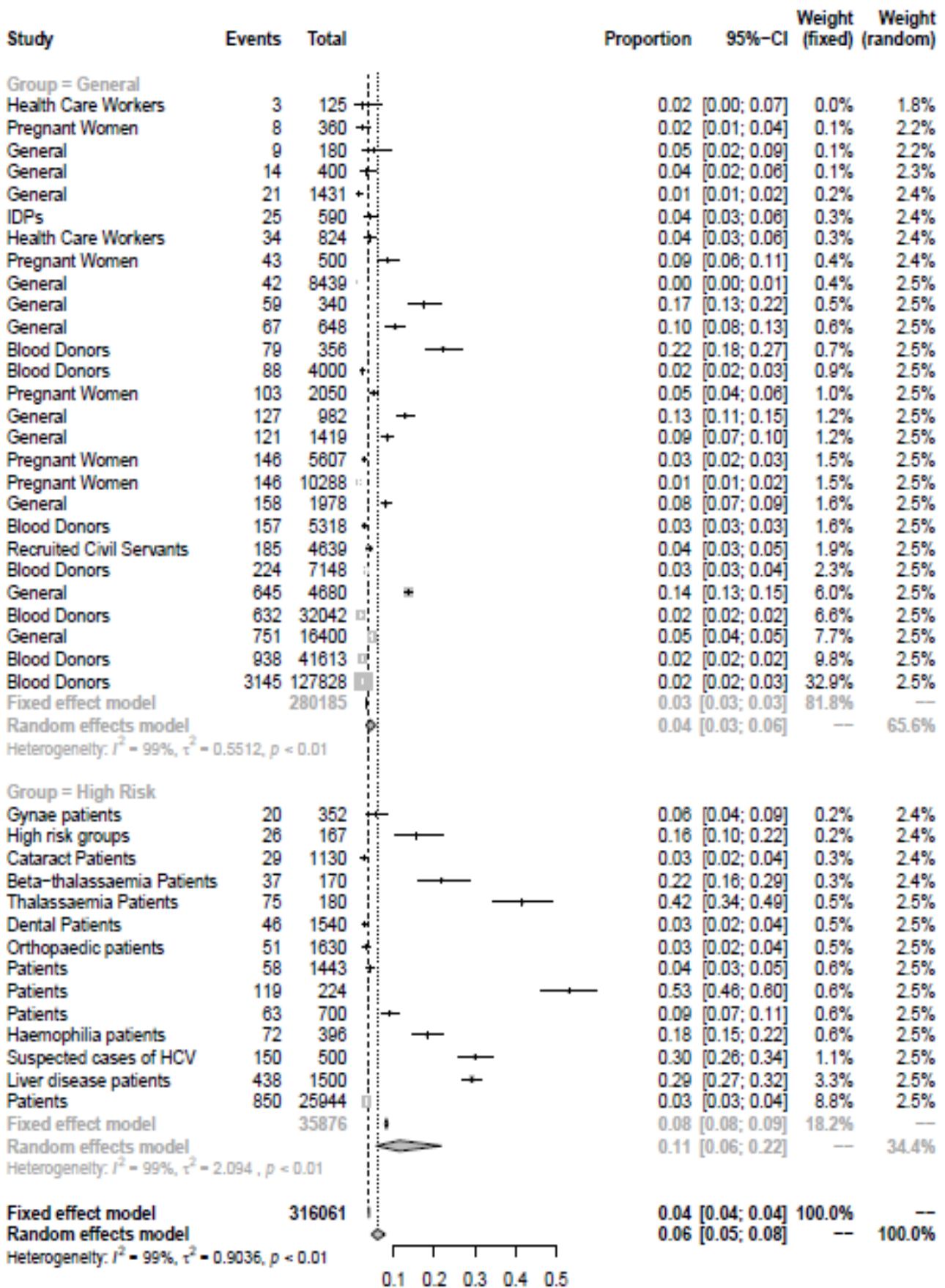**Table 2: Descriptive characteristics of studies reporting HCV prevalence in High-risk population of KP**

High-risk population	Sample size	Male	Female	HCV%	Male (+)	Female (+)	Region	Methods	Reference

Hospital Patients	25,944	13,953	11,911	**3.27%**	554	296	Bannu	ELISA/ ICT	[49]
	1,443	922	521	**4.00%**	39	19	Lakki Marwat	ICT/ELISA	[50]
	700	523	177	**9.00%**	41	22	Mardan	ICT	[51]
	224	124	100	**55.10%**	76	43	Dera Ismail Khan	PCR	[52]
Thalassaemia Patients	180	75	75	**41.70%**	36	39	Peshawar	ELISA	[53]
Multi-transfused Beta-Thalassaemia Major Patients	170	94	76	**21.76%**	21	16	Swat	ELISA	[54]

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Cataract Patients	1,130		2.57 %	13	16	Dera Ismai l Khan	ELISA	[55]
Clinically Suspected Cases of HCV	500	163	337	30 %	53	97	Pesh awar	ICT/ Elisa/ Real-time PCR	[56]
Dental Patients	1,540	561	979	2.98 %	9	37	Pesh awar	ELISA/ ICT	[57]
Gynae Patients	352		352	5.10 %		20	Pesh awar	PCR	[58]
Hemophilia Patients	396	331	65	18 %	63	9	Pesh awar	CMIA	[59]
High-Risk Groups	167	104	63	15.5 7%	18	8	KPK	ICT/ Nested PCR	[60]
Liver disease Patients	1,500	810	690	29.2 0%	210	228	Mard an	ICT/ ELISA/ q-PCR	[61]
Orthopaedic al Patients		1,20		3.12			Abbo		

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	1,630	5	425	%	33	18	ttaba d	ELISA	
									[62]

Figure 2: Forest Plot of studies reporting prevalence of HCV in KP

Study	Events	Total	Proportion	95%-CI	Weight (fixed)	Weight (random)
Group = General						
Health Care Workers	3	125	0.02	[0.00; 0.07]	0.0%	1.8%
Pregnant Women	8	360	0.02	[0.01; 0.04]	0.1%	2.2%
General	9	180	0.05	[0.02; 0.09]	0.1%	2.2%
General	14	400	0.04	[0.02; 0.06]	0.1%	2.3%
General	21	1431	0.01	[0.01; 0.02]	0.2%	2.4%
IDPs	25	590	0.04	[0.03; 0.06]	0.3%	2.4%
Health Care Workers	34	824	0.04	[0.03; 0.06]	0.3%	2.4%
Pregnant Women	43	500	0.09	[0.06; 0.11]	0.4%	2.4%
General	42	8439	0.00	[0.00; 0.01]	0.4%	2.5%
General	59	340	0.17	[0.13; 0.22]	0.5%	2.5%
General	67	648	0.10	[0.08; 0.13]	0.6%	2.5%
Blood Donors	79	356	0.22	[0.18; 0.27]	0.7%	2.5%
Blood Donors	88	4000	0.02	[0.02; 0.03]	0.9%	2.5%
Pregnant Women	103	2050	0.05	[0.04; 0.06]	1.0%	2.5%
General	127	982	0.13	[0.11; 0.15]	1.2%	2.5%
General	121	1419	0.09	[0.07; 0.10]	1.2%	2.5%
Pregnant Women	146	5607	0.03	[0.02; 0.03]	1.5%	2.5%
Pregnant Women	146	10288	0.01	[0.01; 0.02]	1.5%	2.5%
General	158	1978	0.08	[0.07; 0.09]	1.6%	2.5%
Blood Donors	157	5318	0.03	[0.03; 0.03]	1.6%	2.5%
Recruited Civil Servants	185	4639	0.04	[0.03; 0.05]	1.9%	2.5%
Blood Donors	224	7148	0.03	[0.03; 0.04]	2.3%	2.5%
General	645	4680	0.14	[0.13; 0.15]	6.0%	2.5%
Blood Donors	632	32042	0.02	[0.02; 0.02]	6.6%	2.5%
General	751	16400	0.05	[0.04; 0.05]	7.7%	2.5%
Blood Donors	938	41613	0.02	[0.02; 0.02]	9.8%	2.5%
Blood Donors	3145	127828	0.02	[0.02; 0.03]	32.9%	2.5%
Fixed effect model		280185	0.03	[0.03; 0.03]	81.8%	—
Random effects model			0.04	[0.03; 0.06]	—	65.6%
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.5512$, $p < 0.01$						
Group = High Risk						
Gynae patients	20	352	0.06	[0.04; 0.09]	0.2%	2.4%
High risk groups	26	167	0.16	[0.10; 0.22]	0.2%	2.4%
Cataract Patients	29	1130	0.03	[0.02; 0.04]	0.3%	2.4%
Beta-thalassaemia Patients	37	170	0.22	[0.16; 0.29]	0.3%	2.4%
Thalassaemia Patients	75	180	0.42	[0.34; 0.49]	0.5%	2.5%
Dental Patients	46	1540	0.03	[0.02; 0.04]	0.5%	2.5%
Orthopaedic patients	51	1630	0.03	[0.02; 0.04]	0.5%	2.5%
Patients	58	1443	0.04	[0.03; 0.05]	0.6%	2.5%
Patients	119	224	0.53	[0.46; 0.60]	0.6%	2.5%
Patients	63	700	0.09	[0.07; 0.11]	0.6%	2.5%
Haemophilia patients	72	396	0.18	[0.15; 0.22]	0.6%	2.5%
Suspected cases of HCV	150	500	0.30	[0.26; 0.34]	1.1%	2.5%
Liver disease patients	438	1500	0.29	[0.27; 0.32]	3.3%	2.5%
Patients	850	25944	0.03	[0.03; 0.04]	8.8%	2.5%
Fixed effect model		35876	0.08	[0.08; 0.09]	18.2%	—
Random effects model			0.11	[0.06; 0.22]	—	34.4%
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 2.094$, $p < 0.01$						
Fixed effect model		316061	0.04	[0.04; 0.04]	100.0%	—
Random effects model			0.06	[0.05; 0.08]	—	100.0%
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.9036$, $p < 0.01$						

0.1 0.2 0.3 0.4 0.5

Heterogeneity Assessment

The plot (Figure 3) suggested by Baujat pinpoints two studies that are prominent in contributing maximum to the heterogeneity and are the most influential among the studies too [63]. The study by Noor et al (2005) is highly influential while the study by

Nazir et al (2016) show maximum contribution in the heterogeneity, the rest of the studies are lying at the left bottom corner having nominal share on both scales. From the direct observation of the funnel plot (Figure 4 a, b, c) the heterogeneity is quite evident. Not only, but most of the plotted dots are also lying outside the funnel, some of the dots are too far on the right, which causes a significant amount of publication bias (p- value=0.01358). In Group 1 and Group 2 upward bias of magnitude 5 and 8 respectively exists, however, the standard error of the bias is substantial, which consequently makes the publication bias statistically.

Figure 3: Baujat Plot of studies reporting the prevalence of HCV in KP
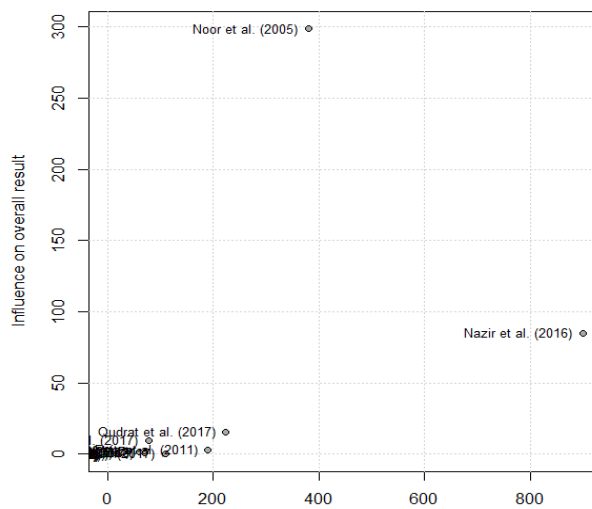
Figure 4: Funnel plot of reporting the prevalence of HCV in KP for (a) All (b) General and (c) High-Risk studies
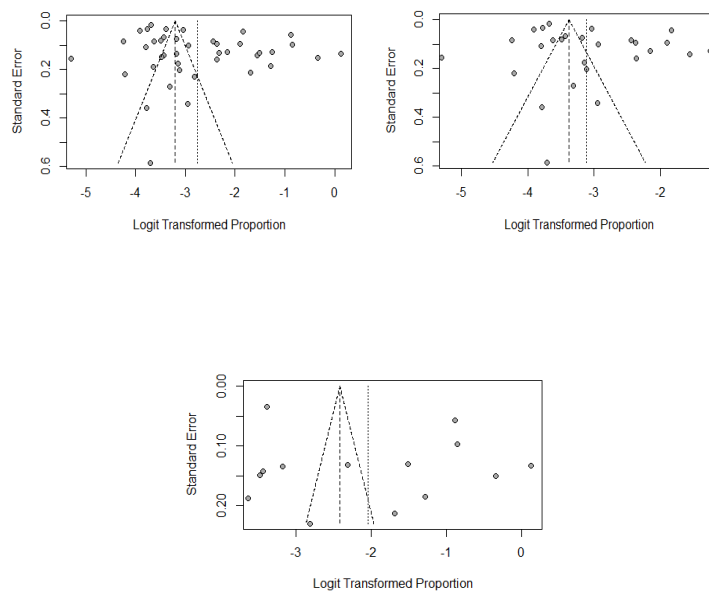
Gender wise comparison

The combined estimate of 26 studies shows that the odds of HCV infection in males as compared to females is fractionally lower for a fixed effect model but the same odds are fractionally higher for the random effect model, however, these odds are lacking in statistical significance (Figure 5). Both Q and I^2 statistics are substantially higher (p-value < 0.0001), indicating a high degree of heterogeneity in gender-wise odds given by these studies. The subgroups analysis based on General and High-Risk Population reveal that when fixed effect model is used for the general population group, the odds are significantly lower (0.78) for a male being affected by Hepatitis C as compared to female whereas in the high-risk population the odds are significantly higher (1.20 times) for male as compared to females. Further, the Q and I^2 statistics reveals significant heterogeneity in both groups of populations. As far as the difference between the two population groups is concerned, it is found from the relevant Q statistics that this is highly significant (p-value< 0.0001). Considering a large amount of heterogeneity in the two groups of populations, it will be sensible to assume a random effect model for analysis. The odds of HCV are fractionally higher in the male as compared to female in both types of populations; however, they are statistically not significant. The heterogeneity, as before, is substantially higher in both groups but between groups comparison now shows the insignificant difference between the two types of populations

Figure 5: Forest Plot of studies reporting gender-wise prevalence of HCV in KP
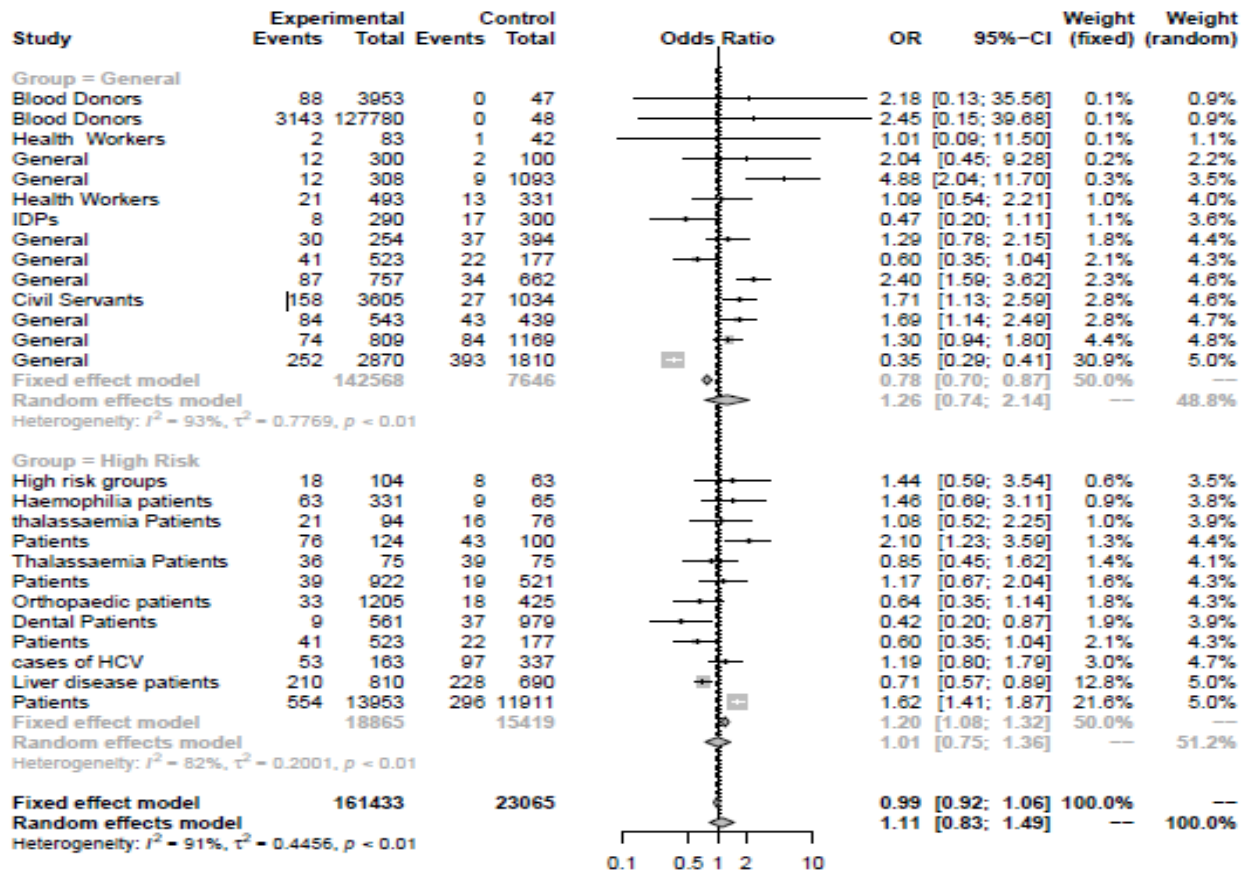
Heterogeneity Assessment

It is evident from the funnel plot (Figure 6a) since the total estimate represents most dots laying close to the central line while a few of them are evenly scattered on both sides of the central line, not causing serious threats to symmetry. Further, in Group 1 it is visible that most dots are laying to the right of the central line, which creates a considerable amount of upward bias, consequently the publication bias and asymmetry is statistically significant (Figure 6b). In Group 2, it is clear that dots are widely scattered, somewhat on the left side,

creating negative bias, however, not attaining statistical significance (Figure 6c). Linear regression test of funnel plot asymmetry (efficient score) and publication bias indicates that there is a bias of magnitude 0.87 but it is statistically insignificant (P-value= 0.45) as the large standard error is substantial (Table 3). The studies of group 1 contain a considerable amount of bias (3.39), which produces significant (p-value = 0.046) asymmetry and publication bias among the studies. The studies of group 2 show the downward bias of magnitude 1.58; however, this amount of bias does not create significant asymmetry and publication in the funnel plot (Table 4)

Table 3: Linear regression test of funnel plot asymmetry for total studies, Group 1, and Group 2

Studies	T	d,f	p.value
All Studies	0.7625	24	0.4532
Group 1	2.2176	12	0.0466
Group 2	-1.3965	12	0.1928

Studies	Bias	se.bias	Slope
All Studies	0.8654	1.1350	-0.1468
Group 1	3.3886	1.5280	-0.8488
Group 2	-1.5848	1.1349	-0.1468

Figure 6: Funnel plot of studies reporting gender-wise prevalence of HCV in (a) All (b) General and (c) High-Risk studies
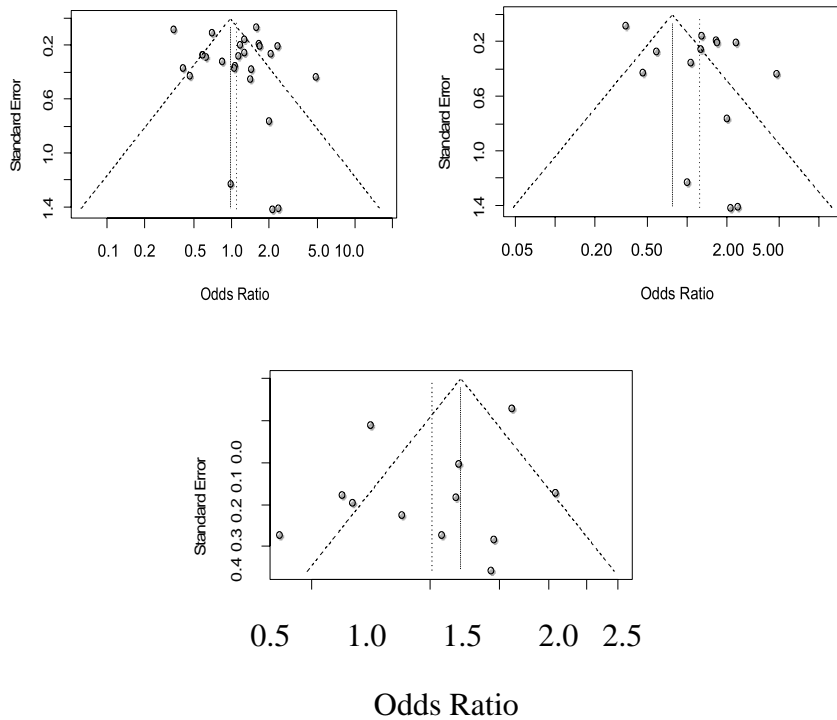
Conclusions

HCV is a major global health problem for both high and low-income countries. This study could serve as a model study of the epidemiology of HCV in a province of a developing country, KP-Pakistan. In a world where advanced countries like Australia, Brazil, Germany, Japan, and the Netherlands have been stated to be on the path to eliminate HCV by the end of 2030, developing countries like Pakistan still struggle with an alarming prevalence rate [64]. Current study emphasizes to the prevalence rate of HCV in a war-affected province of Pakistan, by going through the previously published studies.

Our findings showed that the combined weighted estimate of HCV prevalence in KP is 4% using the fixed-effect model and 6% from the random-effect model. Further, the general and high-risk population have 3% and 8% of prevalence of HCV respectively by fixed effect model and 4% and 11% by random effect model, while comparison between the two groups is highly significant (p-value < 0.0001). These findings are comparable with previously published reports on the prevalence of HCV in Pakistan. Umer et al. (2016) found active HCV infection in approximately 6% of the Pakistani population [25]. Similarly, Arshad et al. (2017) report a prevalence rate of 6.07% in KP and Jiwani et al. (2011) report a prevalence rate of 4.5% to 8% in Pakistan [65]. We noticed that the prevalence of HCV ranges from 1% to 22% in the general population while in high-risk populations it varies from 3% to 53%. Results of our findings are following Memon et al. 2012, which reports the prevalence of HCV in high-risk populations of Pakistan: 25% in health care workers, 10.88% in security personnel, 54.43% in prisoners, and 9.69% in PWID [66]. Similarly, these results are also following Waheed et al. (2009), which reports HCV prevalence of 4.95% +/-

0.53% in the general adult population, 1.72% +/- 0.24% in the pediatric population, 3.64% +/- 0.31% in a young population applying for recruitment, very high 57% +/- 17.7% prevalence in PWID and 48.67% +/- 1.75% in a multi-transfused population [68]. The current study based on General and High-Risk

Population reveal that when fixed effect model is used for the general population group, the odds are significantly lower (0.78) for a male being affected by Hepatitis C as compared to female where, as in the high-risk population, the odds are significantly higher (1.20 times) for the male as compared to the females. Both males and females are vulnerable to HCV and the reason why the odds are significantly higher (1.20 times) for the high-risk male population as compared to the high-risk female population, is maybe due to more exposure of males to the behavioral and social risks (e.g., unsafe injection practices, etc.). This observation is following "The report on Drug use in Pakistan 2013", which states that the male population was found to use more drugs than the female population, and approximately 50% of PWID in KP share syringes regularly [68]. Our findings have some limitations. Most of the previously published data that has been selected for the analysis has a small sample size and is not fully representative of the different populations at risk. Indeed, the lack of information on the age of different sample populations included in the estimates is a clear limitation given the geo-historical relationship between HCV transmission and prevalence across age groups. These qualitative and quantitative limitations of included studies are probably due to high variability within the specifically studied subpopulation, sampling technique, and participant recruitment.

The present study explores and updates current information on the prevalence of HCV in KP. All the basic requirements to deal with HCV are lacking in KP: lack of adequate surveillance systems, appropriate policies, register management, reliable health systems, and adequate public awareness. Pakistan still has no proper system to determine the actual incidence of HCV. The country lacks a proper surveillance system and most of the actual epidemiology data remain unrecorded and unpublished. The Federal Expanded Program on Immunization (EPI) reports that properly functioning surveillance systems are still non-existent. Major problems faced by the country is lack of effective study, disorganization, deficiency of knowledgeable staff and an extremely poor data management. Unless strong public health surveillance systems are not organized and reliable data is not collected, it would be very hard to determine the actual incidence of HCV, and health programs could not accomplish their purpose. HCV infection can be adequately addressed only when the data generated from surveillance systems will be gathered and statistically analyzed [71].

It is important to note that that the knowledge about HCV is quite inadequate among the people of Pakistan. Previous studies have also reported inadequate awareness of causes, vaccination, transmission, consequences, and preventive methods for HCV [29,70,71]. A significant level of public awareness about HCV is very important for fighting disease especially because the people of Pakistan are generally exposed to all sorts of risk factors for transmission of HCV, i.e., the unsafe and reuse syringes, which is the biggest factor contributing to increased HCV in this region [67,72,73]. KP-Pakistan is still struggling with regard to the elimination of HCV. Pakistan needs to take some important steps. First of all, they must establish adequate surveillance systems, able to estimate the epidemiology of HCV. Once collected correctly, the data must be reported and statistically analyzed so that the politicians can draft the policies accordingly. Health sectors should be strictly asked to keep their records and report them to the concerned management. Pakistan also needs adequate health policies that can eliminate all the possible risk factors for HCV transmission. Unregulated blood transfusions still remain a dilemma in Pakistan, country's health systems need to be strengthened Public awareness about HCV is a very important factor for reducing its bioburden; it should be addressed regularly through print and electronic media.

In conclusion, once the actual incidence of HCV infection is accurately determined, the epidemic can be monitored, a high-risk population is identified and the success of interventions be measured [74–77]. HCV treatment and prevention

must become a national priority to reach the WHO HCV elimination targets in Pakistan.

Abbreviations

CMIA= Chemiluminescent microparticle immunoassay

DAA= Direct-acting antiviral

ELISA= Enzyme-linked immunosorbent assay
EPI= Expanded Program on Immunization
HBV= Hepatitis B virus

HCV= Hepatitis C Virus

HDV= Hepatitis Delta virus

ICT= Immunochromatographic test **IDPs=** Internally Displaced People **IMX=** Immunoassay analyzer

KP= Khyber Pakhtunkhwa

MENA= Middle East and North Africa region

ORF= Open reading frame

PCR= Polymerase chain reaction

PRISMA= Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PWID= People who inject drugs

WHO= World Health Organization

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article

Competing interests

The author(s) declare they have no competing interests.

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