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The role of primary prevention in decreasing hcv related disease burden in Pakistan

Abstract

Objective: To identify the most effective primary preventive interventions for reducing the disease burden of HCV infection in Pakistan.

Study Design: Literature Review.

Methods: A comprehensive review of the published literature on the effectiveness of primary prevention interventions to reduce the incidence and prevalence of HCV infection was undertaken by using the scientific data bases.

Results: The review identified 15 relevant studies. These studies identified the key risk factors responsible for high disease burden of HCV infection in Pakistan, that is, therapeutic injections, unsafe medical/surgical practices, needle stick injuries, unscreened blood transfusions, poor knowledge and risk awareness.

Conclusion: There is an immense need of further research and pragmatic guidance for policy makers to evaluate the effectiveness of primary prevention in reducing the transmission of HCV infection. The government of Pakistan and main health authorities should intervene more effectively to control the high rates of HCV infection. Safe injection practices along with safe medical/surgical practices; safe blood supply and risk awareness among the general population should be the main priorities for preventing the spread of HCV infection in Pakistan.

Keywords: Primary prevention; HCV; Pakistan; Risk factors; Disease patterns; Prevalence

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Introduction

Hepatitis C virus (HCV) is a single stranded RNA virus that can cause acute and chronic hepatitis infection. According to World Health Organization (WHO) estimates, the prevalence of HCV in the world is 3%, affecting 170 million people worldwide.[1] Most of the patients although being chronically infected are unaware of this fact as they do not have clinically detectable sign and symptoms.[2] Therefore, they serve as a source of infection to others and are at risk of developing liver cirrhosis and/or liver cancer. WHO has thus, declared HCV as a global public health problem.[3]

The problem of HCV is graver when seen in the context of a developing country like Pakistan. The prevalence of HCV in Pakistan is estimated to be 6%.[4] Eighty percent of the infected individuals in Pakistan develop chronic hepatitis C infection. These high figures clearly indicate how much this disease is posing threat and burden to an already resource strained health care system.

HCV is a blood borne virus and is transmitted through the transfusion of contaminated blood and blood products, unsafe injection practices and inadequate sterilization of medical and surgical instruments in some health care settings. The virus can also be transmitted through sexual contact, and can pass vertically from infected mother to the new born. However, the risk of sexual, perinatal and secondary transmission to household contacts is small. Traditional practices such as tattooing and circumcision with contaminated instruments can also spread HCV infection.

Infection with the virus is associated with an incubation period of 6-7 weeks and clinical illness is asymptomatic with 80% patients are at risk of developing chronic infection that can lead to cirrhosis and liver cancer.[1] Majority of patients only discover that they are infected with HCV, when the disease expresses itself after a long period of time with all its complications. At that point of time, majority of the patients are beyond the scope of treatment and cannot even bear the expenses of treatment.

Interferon injections and some oral direct acting antiviral agents (DAAs) are found effective against HCV infection. In Pakistan, Interferon injections are the most commonly prescribed treatment. It is an expensive drug and is administered several times a week for several months. Moreover many side effects, relapses and remissions with this drug are common.

There is no vaccine and post exposure chemoprophylaxis to prevent HCV infection. Thus, interventions to reduce the possible modes of transmission to protect the healthy population from being infected with this lethal virus are the only protective option available. For this reason, more efforts should be paid to stop the transmission of virus to healthy population than to only relying on treatment of infected population. Therefore, developing effective primary preventive measures is vital in order to prevent and control disease transmission.

The present study is thus designed to analyse literature review to identify effective primary prevention strategies to reduce the HCV disease burden in Pakistan and to make recommendations for more consistent, high-quality and effective primary prevention initiatives.

Methods

The literature was searched using various databases. A variety of keywords regarding the subject were used to identify the relevant literature and selected studies were critically appraised.

Search question

What primary prevention measures against HCV are most useful to reduce HCV related disease burden in Pakistan?

Search strategy

Search strategy was aimed to be sensitive (identification of relevant literature) and specific (exclusion of irrelevant information). Both the factors were influenced by the time period and search terms used in the study. Therefore, there should be a cut-off point between conducting an extensive search (additional resources of information) and a modest research (that can miss some information but do not affect the overall strength of evidence).[5]

Time span of the studies

The time span of literature search depended on the availability of information on the work done for primary prevention of the HCV. For discussion and background evidence, some information was taken from 1985-2010. However, most of the detailed informative data were available from 1996 to 2010. In literature review, studies from 2000 to 2010 were included in literature review because they showed the detailed and relevant information.

Replication of the search results

The search strategy was intended to be clear and transparent with the provision of keywords and search terms used in different databases. This was done so that same results could be replicable by someone else to conduct further research and to improve the results.

Ovid medline and embase

Above mentioned keywords were used in Ovid Medline and Embase databases. Studies were searched from 1996 to 2010.

The cochrane library

The Cochrane Library was used to get the data to address the research question.

Other databases

Web of Science via Web of Knowledge, Science Direct and Google Scholar were also explored to find out the relevant articles and studies by using the same keywords and search sentences.

Inclusion criteria

i. Studies showing primary prevention of HCV infection.
ii. Studies which showed full research material not only abstracts.
iii. Studies in Pakistan were preferred.
iv. Studies from UK and USA were included for comparison of effectiveness of primary prevention in developed world and Pakistan.
v. Studies in English.
vi. Studies In Vivo.

Exclusion criteria

Studies which do not fulfil the inclusion criteria.

Validity of the studies

Validity or quality of study can be assessed by looking on the study design, methodology and analysis of the study (internal validity), also on population, interventions and generalization of results (external validity). Initially those studies were included in the review, which were matched with the inclusion and exclusion criteria and also initial screening questions from the Critical Appraisal Skill Programme (CASP) Assessment Tool.[6] Detailed appraisal of studies was done by using frameworks issued by the National Institute of Clinical Excellence[5] Scottish Intercollegiate Guidelines Network (SIGN) tool[7] and Users guides to the medical literature.[8] These frameworks helped in interpretation of the validity and quality of the studies and also the invention of inferences to inform public health practice and research.[9]

Grade of evidence

Papers were categorized according to the hierarchy of evidence used by the NHS Centre for reviews and Dissemination for epidemiological studies.[9] The grading is shown in the Table 1.

The studies were further assessed by coding system using the frameworks and guidelines issued by NICE[5] and SIGN[7] as shown in the Table 2.

Table 1 Grading of different epidemiological studies

Level	study design
I.	Interventional studies (e.g. randomised controlled trials with allocation concealment)
II.	Quasi-experimental studies (e.g. interventional study without randomisation)
III.	Observational studies with control groups (e.g. case control and cohort)
IV.	Cross-sectional or observational studies without control groups
V.	Bench researches or consensus papers

Table 2 Overall evaluation of the study

Code	criteria
++	Studies which fulfilled all or most of the criteria Where they have not been fulfilled, the conclusions of the study or review are thought very unlikely to alter.
+	Studies which fulfilled some of the criteria Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.
-	Studies which fulfilled few or no criteria The conclusions of the study are thought likely or very likely to alter.

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Results

Implementing the above mentioned search strategy and keywords a total of 189 abstracts and studies were identified from the relevant research literature using the databases mentioned above. Summary of search results is shown in following (Table 3–Table 5).

Table 3 Results of searches with different keywords used in search strategy (Ovid Medline)

S. No.	Keywords	Results
1	Primary prevention.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	39875
2	HCV.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	58843
3	1 and 2	121
4	Primary prevention.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	39875
5	HCV.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	58843
6	Pakistan.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	18139
7	4 and 5 and 6	3
8	Primary prevention.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	39875
9	HCV.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	58843
10	South east asia.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	2715
11	8 and 9 and 10	3
12	Modes of transmission.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	1678
13	HCV.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	58843
14	Pakistan.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	18139
15	12 and 13 and 14	4
16	Primary prevention.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	39875
17	HCV.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	58843
18	UK.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	124761
19	16 and 17 and 18	1
20	Primary prevention.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	39875
21	HCV.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	58843
22	Drug abuse.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	56587
23	20 and 21 and 22	14
24	HCV.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	58843
25	Blood donation.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	4389
26	Pakistan.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	18139
27	24 and 25 and 26	14
28	Disease patterns.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	1605
29	HCV.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, nm, ui]	58843
30	28 and 29	11
31	Prevalence.m_titl.	108976
32	HCV.m_titl.	11831
33	Pakistan.m_titl.	5837
34	31 and 32 and 33	10
35	Riskfactors.m_titl.	77086
36	HCV.m_titl.	11831
37	Pakistan.m_titl.	5837
38	35 and 36 and 37	4

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Table 4 Summary of search results

S. No.	Keywords	Results
1	Primary prevention, HCV	121
2	Primary prevention, HCV, Pakistan	3
3	Primary prevention, HCV, South east Asia	3
5	Modes of Transmission, HCV, Pakistan	4
6	HCV, Primary prevention, UK	1
7	Primary prevention, HCV , Drug abuse	14
8	HCV, Blood donation, Pakistan	14
9	Disease pattern, HCV	11
10	Prevalence, HCV, Pakistan	10
11	Risk factors, HCV, Pakistan	4
12	Total studies	185

Table 5 Search results in cochrane library

S. No.	Keywords	No. of studies
1	Primary prevention of HCV	4

From the total 189 abstracts and studies identified, duplicate studies were excluded, leading to selection of 155 abstracts. Online full literature was available for only 44 studies and rest of 111 studies showed abstracts only. Out of 44, only 15 studies met the inclusion criteria completely and were included for critical appraisal Figure 1. Rest of the 29 studies were not relevant to answer the review question, most of them were unable to describe the effectiveness of primary prevention of HCV, especially in Pakistan. The selected 15 studies showed information about all the provinces of Pakistan and matched completely with inclusion criteria.

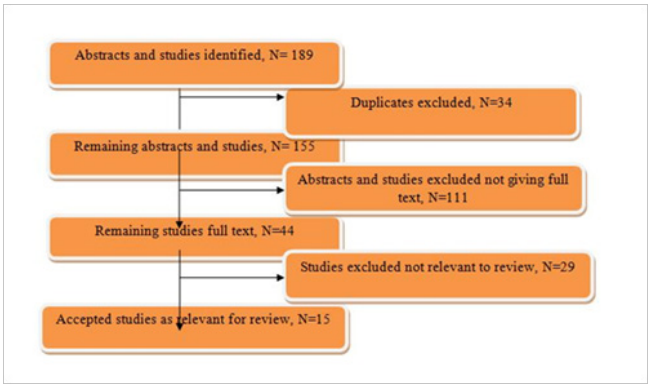

Figure 1 A flow sheet diagram showing papers identified in review.

Out of 15 studies included in the literature review, 12 were cross-sectional studies, 1 was RCT, 1 was case control and 1 was a systematic review. Preference was given to studies conducted in Pakistan. However, most of the available information about Pakistan was based on cross-sectional studies only.

Of the 15 included studies, 11 studies were conducted in Pakistan, 2 in U.K., 1 in U.S.A. and 1 was a systematic review. Studies from U.K and U.S.A. were included to improve and compare the evidence about the key primary preventive measures regarding HCV in Pakistan and the developed world.

Synthesis of research evidence

Research evidence of above mentioned 15 studies indicated following major primary preventive measures to

i. prevent transmission of HCV infection in Pakistan:
ii. Safe medical/surgical practices
iii. Needle and syringe exchange programmes
iv. Screened blood Transfusions
v. Risk awareness
vi. Behavioural and psychological therapy

These studies identified the key risk factors responsible for high disease burden of HCV infection in Pakistan, that is, therapeutic injections, unsafe medical/surgical practices, needle stick injuries, unscreened blood transfusions, poor knowledge and risk awareness (Table 6). It was hard to distinguish the importance of single above mentioned primary preventive measure by individual studies because the studies commented collectively on the effectiveness of above mentioned preventive measures (Table 6). However, most of the studies identified safe medical /surgical practices (e.g. proper prescription of therapeutic injections, professional skills and attitude among doctors and health care workers to avoid needle stick injuries (NSI) and use of sterilizes equipments in hospitals and clinics), needle/ syringe exchange programmes and screened blood transfusions as the most important primary preventive measures in order to control HCV infection in Pakistan.

Discussion

The evidence suggested that current primary preventive interventions are insufficient in reducing transmission of HCV infection in Pakistan. The incidence and prevalence of HCV infection in Pakistan are quite high despite the implementation of different apparent primary preventive programmes. The following key primary preventive measures would be helpful in decreasing HCV transmission in Pakistan.

Safe medical/surgical practices

The most important primary preventive strategy for reducing HCV infection, as evident from literature, is safe surgical and medical practices. In Pakistan, most of the clinicians prescribe unnecessary therapeutic injections for common ailments that can be treated with oral medications.[10–12] Unsterilized medical/surgical equipment,[13] and lack of professional skill and attitude of health care workers[12] are other major components of unsafe medical/surgical practices.

By encouraging safe medical/surgical practices, incidence of HCV infection can be significantly decreased. This will also reduce the vertical transmission of HCV from mother to new born by least affecting the females from gynaecological procedures.[14–16] However, it needs the active involvement of public health officials and higher authorities like Ministry of Health in federal and provincial governments.[17]

Needle and syringe exchange (NSE) programmes

Another important primary preventive intervention was found to be needle and syringe exchange (NSE) programmes. A high population of IDUs was reported in Pakistan.[18] Kuo et al.[19] in a study, showed HCV prevalence of 93% and 75% among IDUs of Lahore (Punjab) and Quetta (Balochistan), respectively, while Achakzai et al.[20] in a

smaller study in 2004, showed HBV, HCV, and HIV prevalence of 6%, 60%, and 24%, respectively, in the IDUs of Quetta [19,20]. A follow-up national survey in 2005 showed HIV prevalence of 23% and 0.5% and HCV prevalence of 88% and 91% in IDUs of Karachi (Sindh) and Lahore (Punjab), respectively.[21]

Evidence showed that needle and syringe exchange programmes can significantly decrease the transmission of HCV infection in Pakistan.[19,22–24] However, implementation of this programme in a developing country like Pakistan requires political legitimacy and evaluation of cost-effectiveness of large scale NSE programmes. According to a report published by The Commonwealth Department of Health and Ageing of Australia, NSE is a cost effective programme in reducing the incidence of HCV infection.[25] This report also indicated that NSE showed an effective return on financial investment by government, calculated at a lifetime saving to costs of treatment of $3,653 million Australian dollars in treatment costs.[2]

Screened blood transfusions

Most of the people in Pakistan are unaware of consequences of unscreened blood transfusions.[16,26] Adding to the misery, most of the blood banks and hospitals also ignore the significance of screening the blood products and blood donors.[26]

In another study, Luby et al. researched 24 randomly selected blood banks in Karachi; 95% of the banks had diagnostic facilities to test for HBV and HCV but only 23% could screen for HCV and 55% for HIV.[27] Fifty percent of the donated blood was taken from paid blood donors and only 25% from voluntary blood donors. More recent data about the practices were not available. In 2001, Ahmed carried out a study to estimate the seroprevalence of HCV in blood donors and revealed a higher prevalence of Hepatitis B in professional blood donors as compared to voluntary blood donors (9% vs. 0.8%, $p< 0.001$).[28]

Screening of blood donors and blood products for HCV infection can be an effective preventive intervention in reducing the incidence and transmission of HCV infection but it requires implementation of more authentic legislations.[13,15,16,26]

It is also found that most of the epidemiological studies focussed on blood donors only to estimate major risk factors for HCV transmission in Pakistan. Although it was a good and easy attempt to have an idea about prevalence of HCV infection, but blood donors did not represent the general population. In such studies, most of the study participants were males and researchers had not provided data about females.[15] Therefore, more studies were required which focussed on general population to estimate common risk factors responsible for disease transmission.

Risk awareness

In Pakistan, most of the people are unaware of risk of getting not only HCV infection but also other blood borne infections like Hepatitis B and HIV. In this aspect, non-sterilized practices done by barbers are a major risk factor of high HCV incidence in males.[15] Population attributable risk for face and armpits shaves by barbers is 29.4 and 33.6%, respectively.[16] Risk of HCV infection is 5.1 times more in males who have face shaves by barbers as compared to those who do not shave by barbers.[16] Therefore, risk awareness and proper education for men may result in considerable decrease in HCV transmission in Pakistan. This aspect should be taken into account while devising a primary preventive programme in Pakistan. Other less common risk factors include ear and nose piercing in females.[15] There is thus, an immense need of educating the people about the risks and consequences of HCV infection.[13–16,29]

Behavioural and psychological therapy

The effectiveness of behavioural and psychological therapy was found to be significantly associated with decrease in HCV transmission.[17,30] Different studies conducted in developed countries like UK suggested that behavioural and psychological therapy is an effective intervention to control HCV related mortality and morbidity.[31] But this intervention is mainly focussed on certain target groups like IDUs. In order to get a wider change in general population, risk awareness programmes should be adapted and promoted.

Limitations of the study

This results of this study need to be considered in context of following limitations:

a. There was limited robust literature to find out the effectiveness of major primary preventive interventions in reducing HCV related disease burden in Pakistan.

b. Most of the studies included in this study were cross sectional. The validity of cross sectional studies is threatened because of their susceptibility to selection bias, misclassification bias and confounding. Although there was desire to include more randomized controlled trials and analytical studies, but most of the informative data about Pakistan were available by cross sectional studies.

c. There was not enough informative data available about Pakistan. On some places, where it found to be appropriate, studies from UK and USA were used to support the argument.

Ethical approval

As this paper was a literature review only and no personal identifiers were used in the study, therefore, no ethical approval was required.

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Conflicts of interest

The authors have no conflict of interest for this research.

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