REASSESSMENT OF SELECTED HEALTHCARE ASSOCIATED RISK FACTORS FOR HBV AND HCV INFECTIONS AMONG VOLUNTEER BLOOD DONORS, KARACHI, PAKISTAN

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SUMMARY

Epidemiologic studies conducted in the 1990s identified several independent healthcare associated risk factors for HBV and HCV infections in Pakistan. In 2002, we re-examined healthcare associated HBV and/or HCV infection risk factors in volunteer blood donors.

In this case-control study, we collected data using a structured questionnaire on socioeconomic attributes, putative healthcare related risk factors, and other known factors for HBV and HCV infections in Karachi, Pakistan.

The multivariable logistic-regression model (166 cases, 394 controls) after adjusting for socio-demographic attributes and other known HBV and HCV risk factors revealed that more cases than controls had multiple lifetime hospitalization, adjusted odds ratio (AOR)=2.48; 95% confidence interval (CI) 1.04,5.94, and had received dental treatment from an unqualified provider (AOR=5.90, CI, 1.66,21.02). More cases than controls had received a large number of therapeutic injections during the last 5 years (1–5 injections vs. 0, AOR=2.64, 95% CI 1.06,6.60; 6–19 injections vs. 0, AOR=4.09, 95% CI 1.59,10.51; ≥20 injections vs. 0, AOR=4.34, 95% CI 1.70,11.07), and had their last injection given using a re-usable glass syringe (AOR=3.41 CI 1.13,10.29).

Our data suggest that risk factors for HBV and HCV infections identified in the last decade have remained unchanged in healthcare facilities in Karachi. Additional multi-disciplinary efforts are needed to control healthcare associated HBV and HCV transmission in Pakistan.

Key words: healthcare, hepatitis B virus, hepatitis C virus, risk factors, blood donors, developing countries, Pakistan

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INTRODUCTION

Inadequate infection control practices in healthcare settings have been shown by epidemiologic investigations, to contribute significantly to the global burden of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. This is particularly true in developing countries around the world such as Pakistan (1–3).

Historically hepatitis has been a menace across the world without regards to geographical boundaries, socio-cultural and economic divide. Recognizing this problem, the universal guidelines for infection control were developed in late 1980s (4), and their implementation in the developed nations has led to the application of rigorous infection control practices in healthcare settings. In conjunction with quality assurance systems, higher occupational safety standards, and greater recognition of and respect for patients’ rights, the universal precautions have resulted in a dramatic improvement in infection control (1, 5). The situation in developing countries such as Pakistan, however, remained unchanged, as standardized infection control did not become widely implemented and/or practiced (6).

Observational studies conducted in the past decade identified parenteral exposures in healthcare settings, including the use of unsterile medical or dental equipment, and intramuscular (IM) and intravenous (IV) therapeutic injections, as major contributors to HBV and HCV infection cases in Pakistan (7–9). In Pakistan, it wasn’t until mid 1990s that the efforts were initiated by public health legislators, healthcare providers, and communities towards implementation of several infection control and prevention measures to reduce healthcare associated infections including HBV and HCV. An integral part of these efforts were advocacy for campaigns for HBV vaccination. (10).

Several years have passed since initiation of these efforts that, common sense dictates, must have had some impact on practices that were previously found to contribute to spread of HBV and/or HCV infections in Pakistan. However, no or minimal efforts have been made to gauge the impact of these efforts, or to quantitatively assess the current magnitude of healthcare associated risk factors for HBV and HCV infections.

The relative importance of the modes of transmission of an infectious disease can change over time, particularly when rejuvenated efforts are made to control its spread. The periodic evaluation of the common modes of transmission of a disease is therefore important, as it not only helps public health officials in developing specific prevention and control strategies for a given transmissible infection, but also helps to evaluate the impact of such control strategies.
Quantitative data regarding the transmission of HBV and HCV in healthcare settings are needed in order to design an evidence-based optimal infection control strategy in healthcare settings in Pakistan. This research was a secondary analysis of a large case-control study and carried out as a post-implementation assessment of infection control practices by reevaluating the healthcare associated risk factors for HBV and HCV infections reported in earlier investigations in Pakistan. This paper is an effort to help fill this gap in understanding of the current status of risk factors of HBV and/or HCV and to indirectly assess the impact of infection control practices and campaigns on previously identified risk factors, for HBV and/or HCV infections.

MATERIALS AND METHODS

Study Setting, Population and Subject Recruitment

The methodological details of the primary study have been described elsewhere (11) and are briefly outlined here. This case-control study was carried out in 2002 in Karachi, the largest city of Pakistan with a population of over 14 million. The study was conducted at two large blood banks in Karachi that collect blood donations from only non-remunerated volunteers. Both blood banks follow similar donor criteria and exclude potential donors during the screening process who admit known risk factors of transfusion transmissible infections or any medical/non-medical condition associated with high risk, such as use of narcotic drugs, jaundice in the past 5 years, and recent hospitalization. Male blood donors aged 18–64 years who donated blood were contacted after obtaining addresses and phone numbers from the blood banks’ records. Both blood banks used commercially available enzyme-linked immunosorbent assay (ELISA-III) kits to test for seropositivity against HBV (HBsAg) and HCV (HCV-antibody) in donated blood.

Cases and Controls

Case subjects were blood donors found seropositive for HCV antibody and/or HBsAg in the blood banks’ records between October 2001 and March 2002. The identified donors were contacted and explained the purpose of the study and requested to donate a fresh blood sample. The fresh blood samples were re-tested and only blood donors who were positive for HCV and/or HBV on the second sample were considered cases. The control group included HCV and HBV seronegative blood donors from the same blood banks. We excluded cases and controls testing reactive for other transmissible diseases such as human immunodeficiency virus (HIV) and malaria.

Questionnaire Development, Subject Recruitment and Interview Procedure

An in-person interview with each study subject was conducted using a structured questionnaire on demographic and socio-economic characteristics (e.g., age, ethnicity, education, income), various potential exposures to blood or blood products (e.g., history of hospitalization, therapeutic injections/intravenous infusions received), sexual activity (e.g., number of sexual partners), and household exposure to hepatitis (e.g., history of hepatitis in a family). We included questions that could provide quantitative data regarding HBV and HCV risk factors: lifetime number of hospitalizations, number of dental treatment received during the last 5 years, and number of intramuscular (IM) and intravenous (IV) injections received during the last 5 years. The questionnaires were administered through trained interviewers.

Ethics

Prior to interview, each potential study subject provided verbal informed consent. The Institutional Review Committee (IRC) for human research at the Aga Khan University approved the protocol.

Statistical analysis

A database was developed in Epi Info (CDC version 6.0, 1996) for data entry, cleaning and management, while all analyses were performed using SAS1 software version 9. Frequencies of all the categorical variables were computed for cases and controls. Crude odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using logistic regression, relating each factor with HCV and/or HBsAg positive status. To examine the independent con-

Table 1. Socio-demographic characteristics of cases and controls enrolled to assess healthcare care associated HBV and/or HCV risk factors in Karachi, Pakistan

<table>
<thead>
<tr>
<th></th>
<th>Case (n=166)</th>
<th>Control (n=394)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (completed years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–25</td>
<td>57 (34.3)</td>
<td>212 (53.8)</td>
</tr>
<tr>
<td>26–40</td>
<td>93 (56.0)</td>
<td>159 (40.4)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>16 (9.7)</td>
<td>23 (5.8)</td>
</tr>
<tr>
<td>Formal schooling (completed years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>30 (18.1)</td>
<td>98 (24.9)</td>
</tr>
<tr>
<td>1–10</td>
<td>59 (35.5)</td>
<td>101 (25.63)</td>
</tr>
<tr>
<td>11–12</td>
<td>29 (17.5)</td>
<td>56 (16.71)</td>
</tr>
<tr>
<td>&gt;12</td>
<td>38 (26.9)</td>
<td>137 (34.77)</td>
</tr>
<tr>
<td>Profession/occupation</td>
<td></td>
<td></td>
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<tr>
<td>Student</td>
<td>19 (11.5)</td>
<td>70 (17.77)</td>
</tr>
<tr>
<td>Self employed/Office worker</td>
<td>95 (57.2)</td>
<td>194 (49.24)</td>
</tr>
<tr>
<td>Manual worker/Un-employed</td>
<td>52 (31.3)</td>
<td>130 (32.99)</td>
</tr>
<tr>
<td>Household income (PKR*/month)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;15,000</td>
<td>19 (11.5)</td>
<td>54 (13.71)</td>
</tr>
<tr>
<td>8,001–15,000</td>
<td>60 (36.1)</td>
<td>97 (24.62)</td>
</tr>
<tr>
<td>5,001–8,000</td>
<td>25 (15.1)</td>
<td>62 (15.74)</td>
</tr>
<tr>
<td>≤5,000</td>
<td>42 (25.3)</td>
<td>102 (25.89)</td>
</tr>
<tr>
<td>Refused to answer</td>
<td>20 (12.0)</td>
<td>79 (20.05)</td>
</tr>
</tbody>
</table>

*PKR: Pakistani rupees (1 $ =~ 60 PKR, in 2002)

1 The analysis for this paper was generated using SAS/STAT software, Version 9. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, US

32
distribution of each healthcare associated risk factor for HBV and/or HCV infections, a multivariable logistic regression (MLR) model was developed, and adjusted ORs (AORs) with their respective 95% CIs were computed.

RESULTS
A total of 166 cases and 394 controls were enrolled during the study period. The socioeconomic and demographic characteristics of cases and controls are presented in Table 1. When adjusted for socio-demographic characteristics and known risk factors for HBV and/or HCV, the final MLR model revealed that more cases than controls had at least 1 lifetime hospitalization, AOR=2.48; 95% CI, 1.04, 5.94, and had received dental treatment from an unqualified provider, AOR=5.90, CI, 1.66, 21.02. More cases than controls also had received a large number of therapeutic injections during the last 5 years (1–5 vs. 0, AOR=2.64, 95% CI, 1.06, 6.60; 6–19 vs. 0, AOR=4.09, 95% CI, 1.59, 10.51; ≥20 vs. 0, AOR=4.34, 95% CI, 1.70, 11.07), and had their last injection given using a reusable glass syringe (AOR=3.41 CI, 1.13, 10.29) (Table 2).

DISCUSSION
This study reassessed selected healthcare associated risk factors for HBV and HCV infections identified during the past decade in Pakistan. Our analysis identified several factors that were associated with HBV and/or HCV infection. Case patients were significantly more likely to report multiple lifetime hospitalization as compared to controls. This finding is consistent with reports in literature that found such an association in developing countries (12, 13). This finding even after a decade of introduction of the standardized infection control practices indicate towards an improper implementation of these measures.

Therapeutic injections received at healthcare facilities have been reported as the major risk factor for both HBV and HCV infection in the developing world. Similar to earlier reports (6, 7, 13, 14), our data showed a positive association between a large number of IM injection received in the past five years and HBV and/or HCV seropositive status. A dose-response gradient between the number of IM injection received and HBV and/or HCV seropositive status was also observed, i.e., the number of IM injections received in the past five years increased, as the odds of being HBV and/or HCV seropositive increased.
Luby et al. (7) were among the first in Pakistan to provide empirical evidence of the association between frequent therapeutic IM injections and the spread of HBV and HCV infections from an epidemiological study in Punjab, Pakistan. This situation has remained unchanged as evident from findings of subsequent studies (14, 15). Replication of these findings in our study is another indicator that no major changes have occurred over time. Even more recently it has been estimated that an average Pakistani receives an estimated 13.6 injections per year (14), and that majority of these injections are administered under unsafe conditions (16), exposing the patient to several blood borne pathogens, including HBV and HCV.

Importance of injections in spreading blood transmittable diseases such as hepatitis is well documented (17, 18). The availability of injectable medications and equipment without a physician’s prescription further compounds this problem (5).

Individuals with HBV and/or HCV infection were more likely to report receiving dental treatment from unqualified providers. Dental practice by unregistered and unqualified providers is not uncommon in developing countries, including Pakistan. Investigations have shown an association between unqualified dental care provider and HBV and HCV infections (19, 20). These providers are un-aware of infection control practices and often use unsterilized instruments. Additionally the infection control initiative in Pakistan focused exclusively on registered and legal health care providers and establishments, thus we didn’t expect and were not surprised by seeing dental care by unqualified person to be a continuing risk factor of HBV and/or HCV infections.

A few limitations of our study are worth mentioning. Our findings’ generalizability is limited to the male volunteer donors. However, since no sex-specific risk factors for healthcare associated HBV and HCV infections were identified, we expect our findings to be applicable across both sexes. Additionally, any public health measure in blood donors will likely have most success when it targets males, as a vast majority of blood donors in Pakistani culture are males. Since, we collected the data retrospectively using a case-control study design (21), it is not possible to completely avoid or eliminate recall bias. However, all of the factors that we explored and they were retained in the final multivariate model were health care related and clearly defined, involving simple recall. We therefore expect recall inaccuracies to be similar in both groups and not different based on case or control status of the patients. The resultant ‘bias’ if any would make our estimates a little conservative but valid. All risk factor data were generated by self-reports. Therefore, participants may have responded cautiously to questions about culturally sensitive high-risk behaviors, such as extra-marital sexual activities; leading to under-reporting and underestimation of some risk behaviors. However, we expect this under-reporting to be similar for both cases and controls and any resultant response bias, would be non-differential in nature. Therefore, the observed exposure disease relationship may be more conservative but still valid. For HCV evaluation, we used HCV antibody as a serological marker, which only indicates prior exposure to HCV and does not specify the duration of infections. We used HBsAg for the evaluation of HBV infection; which, in the majority of infected individuals is not detectable 4–6 weeks post infection. This guarantees accurate recruitment of HBV cases as per our case definition, but leaves open the possibility that some of our controls might have been infected with HBV in the past and may not have been true controls. This again might have lead to under-estimation of strength of association of some factors but it doesn’t threat the validity of our findings.

Our method of combining HBV and HCV cases in our outcome variable and obtaining a single effect size for both infections may be considered unconventional by some. However, since our objective was to identify healthcare related risk factors for HBV and HCV, and both infections are efficiently acquired through parenteral exposures and also share similar transmission routes in healthcare settings, we consider this combination justifiable. Although we collected data on several types of parenteral exposures associated with healthcare facilities (e.g., number of IV injections received in the last one, five, and ten years, and body injury requiring consultation with a doctor), the strong correlations (p<0.05) among these variables (multicollinearity) restricted our variable selection. The final MLR model was therefore restricted to the variables that best explained our outcome of interest.

Conclusion

In conclusion, our data suggest that risk factors for HBV and HCV identified in the last decade have remained unchanged in healthcare facilities in Karachi. Despite recent control efforts, inadequate infection control practices in healthcare settings seem to continue to play a role in the spread of HBV and HCV in Pakistan. This suggests that proven effective infection control measures, though introduced, have not been successfully implemented, in general. Effective implementation of these measures can significantly reduce the risk of transmission from parenteral exposures through unsterile medical or dental equipment, and particularly IM therapeutic injections. Additional multi-disciplinary efforts involving legislators, healthcare professionals, and communities are needed to control healthcare associated HBV and HCV transmission in Pakistan and similar developing countries.

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REFERENCES

The Anna Lindh Programme on Conflict Prevention published already two books of articles on topics of prevention of conflicts in the modern world: in 2004 on developing a culture of conflict prevention, and in 2005 on development, security and conflict prevention. In the 2006 issue there are discussed countless connections between conflicts and health.

There are many different layers of the problem, which are not recent: already in the first introductory part Javier Solana quotes the American microbiologist and epidemiologist Hans Zinsser that the historically common infectious diseases as typhus, plague, cholera, typhoid fever or dysentery decided more military campaigns than Hannibal, Caesar or Napoleon. Disease can cause social instability – a good example are contemporary epidemics of HIV/AIDS of 2004, and SARS epidemics which only few months later endangered not only health but also the economic stability of many countries, creating also new opportunities, as states in his chapter David Hamburg. Poverty reduction could have an important impact on national health. Health seems to be important in future contents of diplomacy and can also create the bridge to peace in many countries and regions of the world. Both health and development can prevent violent conflict, an orientation toward education is an important part of such activities. Education is one of the important underpinnings of successful developmental policies. Educational policy has to involve also women which is one of the important underpinnings of successful developmental policies.

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