Author's response to reviews

**Title:** Epidemiology of the human immunodeficiency virus in Saudi Arabia; 18-year surveillance results and prevention from Islamic perspective.

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Editor
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Re: MS 196784755296542 for BMC Infectious Diseases

Dear Editor

It was a real pleasure to have received your letter dated 6 May 2004 requesting a revision of the above manuscript taking into consideration the valuable suggestions of the two reviewers and the editorial comments.

The manuscript has been entirely revised according to the reviewers’ and the Editor’s recommendations as follows.

Reviewer 1: John Martin M Kaldor

Introduction

Perhaps it would be helpful to give a very brief description of Saudi Arabia, including total population, main population centers, and administrative structure.

Authors’ response
As suggested, a brief paragraph was added to the introduction (after the 1st paragraph) to describe Saudi Arabia as follows: Saudi Arabia occupies most of the Arabian Peninsula with an area of about 2,240,000 sq km (figure 1). It comprises 13 administrative provinces, namely, Makkah province (which includes the holy city of Makkah, Jeddah and Tayef), Madinah province (which includes the holy city of Madinah), Riyadh province (which includes the capital city Riyadh), the Eastern province (which includes Dammam, Ahsa, and Hafr Albaten), Asir province (which includes Abha and Bisha), Jof province (which includes Jof and Qerayyat), and Baha, Jizan, Najran, Hail, Hudud Shamaliyah (North borders), Qassim, and Tabook provinces. The capital and largest city is Riyadh. The population in Saudi Arabia is 24,293,844, including 5,576,076 non-nationals as estimated in July 2003. Approximately, 42.3% of the population is below 15 years of age, 54.8%, between 15 and 64 years, and 2.9%, above 64 years of age. Ninety nine percent of the population is Muslim and the country is governed according to the Islamic law.

Methods

Some more detail on surveillance methods would be useful. Are reports by name, or by code?

Authors’ response
The following sentence was added in “Patients and Methods, paragraph 1, line 15” as follows: All HIV infections diagnosed in governmental or private health care facilities are notified to the Ministry of Health (MOH) using unique identifying codes.
How is the information on mode of transmission obtained?
Authors’ response
The following sentence was added in “Patients and Methods, paragraph 2, line 1”:
Epidemiological data are collected from patients by the attending physicians on standardized data collection forms. The likely mode of transmission is determined by the attending physician after interviewing the patient and taking complete history regarding high risk behaviors. The mode of transmission is considered to be unknown if the patient fails to admit to any high risk behavior.

Are overseas workers tested routinely on arrival in Saudi Arabia?
Authors’ response
The following sentence was added in “Patients and Methods, paragraph 1, line 6” as follows:
In addition to being HIV tested in their homeland as a compulsory prerequisite for employment in Saudi Arabia, expatriates are routinely retested for HIV upon arrival to Saudi Arabia before they are allowed to work and then regularly every 2 years to have their legal residence permits renewed. Only HIV-negative expatriates are allowed to work in Saudi Arabia.

Results
A map would be helpful
Authors’ response
A map was added (figure 1) and the original figures 1 and 2 were renamed as 2 and 3.

Is there any information on how many HIV tests were carried out by region?
Authors’ response
Unfortunately no.

Because of the potential variation in the extent of testing, it would be useful to see a separate analysis of time trends, sex and risk factors that was restricted to AIDS cases only.
Authors’ response
We are sorry, this analysis can not be readily done.

The proportion of Saudi women with HIV seems quite high. Is there any indication of transmission mode breakdowns by sex and Saudi/non-Saudi origin?
Authors’ response
Yes, there is. The following paragraph was added in the Results section, line 3 to clarify this point:
The likely mode of HIV transmission among 340 Saudi infected female patients was as follows: blood transfusion, 86 (25.3%) patients; marital sex, 74 (21.8%) patients; maternal transmission to female babies, 27 (7.9%) patients; non-marital sex, 8 (2.4%) patients; intravenous drug abuse, 3 (0.9%) patients; and in the remaining 142 (41.7%) patients the mode of transmission was unknown. Among 1376 non-Saudi HIV infected female patients, the likely mode of transmission was as follows: non-marital sex, 209 (15.2%) patients; blood transfusion, 32 (2.3%) patients; marital sex, 4 (0.3%) patients; intravenous drug abuse, 3 (0.2%) patients; maternal transmission to female babies, 3 (0.2%) patients; and in the remaining 1125 (81.8%) patients the mode of transmission was unknown.
In the Discussion section the following sentence was added to paragraph 2 line 7 [The vast majority of Saudi HIV-infected women with identifiable risk factors acquired the infection through blood transfusion or marital sex with their infected husbands.]

Table 2: Presumably the prevalence is the cumulative prevalence of diagnosis per 100 000 total population. If so, what year is the population drawn from, or is it an average over the time period?
Authors’ response
Yes, indeed, it is the average population over the surveillance period

Is it possible to analyze prevalence separately for Saudi/non-Saudi, ie are there denominator data available on these populations either nationally or by region?
Authors’ response
Unfortunately no data available on the census of non-Saudi population by region. Therefore such information can not be obtained.

Table 3: Are any prevalence data available by group tested, eg for tuberculosis patients, blood donors, surgical patients?
Authors’ response
Unfortunately no.

Figure 2: Presumably by year of HIV diagnosis (not transmission as implied by the title).
Authors’ response
You are right. The title of the figure was corrected as follows: [Figure 3: Number of HIV infections transmitted through blood transfusion by year of HIV diagnosis in Saudi Arabia from 1984 through 2001] and the corresponding sentence in the Results section, paragraph 3 was rephrased as follows: [Figure 3 shows the annually reported number of HIV infections transmitted by transfusion of blood or blood products by year of HIV diagnosis from 1984 through 2001. The number of these infections has declined to zero by year 2001. All such infections were due to transfusions administered to patients before 1986.].

Discussion
This section presents a number of interesting issues "from [an] Islamic perspective", to quote the article's title. However it might be reasonable for the authors to note the heterogeneity of both doctrine and practice across Islamic societies.
Authors’ response
The following sentence was added at the end of paragraph 8 in the Discussion section to emphasize this point [It should be noted, however, that HIV preventive strategies in some Islamic countries do not necessarily abide by the Islamic doctrine and that knowledge, attitude, and practice of Muslims in various Islamic societies do not necessarily conform to Islamic norms.]
The first paragraph makes reference to higher numbers of HIV diagnoses in expatriates and regions where expatriates live. This section should note the possibility that testing rates might be higher among expatriates, and give relevant data on testing if they are available.

**Authors’ response**

The following sentence was added to the first paragraph, line 2, to address this point: [Expatriates are routinely tested for HIV upon arrival to Saudi Arabia and then regularly every 2 years to have their legal residence permits renewed. Therefore, one possible explanation for the higher prevalence of HIV infections among expatriates is that HIV testing rates might be higher among expatriates compared to Saudi citizens.].

Unfortunately we do not have data on the number of HIV tests done for Saudi and non-Saudi patients to support this speculation.

**Third paragraph should note that some countries in both Asia and Africa appear to have had success in reducing levels of transmission.**

**Authors’ response**

The first sentence in this paragraph was amended to address this point as follows [The international efforts to control the HIV pandemic have failed to control it on a global scale despite their partial success in many of the developed countries and some of the developing countries.].

In the same paragraph, the last sentence seems to imply that transmission in developing countries is due to the lack of antiretroviral therapy.

**Authors’ response**

The last sentence was rephrased to address this comment as follows [Additionally, the limited access to antiretroviral medications in the underdeveloped countries has compounded the problem and perhaps contributed to some extent to the spread of HIV from untreated patients to new victims.].

**Fifth paragraph (p 12): It has been well documented in both Asia and Africa that a substantial amount of transmission occurs within married couples, generally from male to female. In some countries this is probably the main pathway of HIV transmission.**

**Authors’ response**

Yes, there is. The following paragraph was added in the Results section, line 3 to clarify this point: [The likely mode of HIV transmission among 340 Saudi infected female patients was as follows: blood transfusion, 86 (25.3%) patients; marital sex, 74 (21.8%) patients; maternal transmission to female babies, 27 (7.9%) patients; non-marital sex, 8 (2.4%) patients; intravenous drug abuse, 3 (0.9%) patients; and in the remaining 142 (41.7%) patients the mode of transmission was unknown. Among 1376 non-Saudi HIV infected female patients, the likely mode of transmission was as follows: non-marital sex, 209 (15.2%) patients; blood transfusion, 32 (2.3%) patients; marital sex, 4 (0.3%) patients; intravenous drug abuse, 3 (0.2%) patients; maternal transmission to female babies, 3 (0.2%) patients; and in the remaining 1125 (81.8%) patients the mode of transmission was unknown.]
In the Discussion section the following sentence was added to paragraph 2 line 7 [The vast majority of Saudi HIV-infected women with identifiable risk factors acquired the infection through blood transfusion or marital sex with their infected husbands.]

In the same paragraph, what is the evidence that drug use is increasing in Saudi Arabia?

Authors’ response

Unfortunately the official information on drug abuse in Saudi Arabia is kept confidential and not for public use. Some of this information (cited as unpublished data) and the few published studies on this subject have been summarized in a new paragraph (paragraph 4) in the Discussion section as follows [Substance abuse is an increasing problem in Saudi Arabia as it is in the rest of the world [3]. Substances abused include injectable drugs such as heroin and cocaine and non injectable drugs such as cannabis and amphetamine-type stimulants. The estimated annual prevalence of heroin and amphetamine abuse in Saudi Arabia in 2000 as percentage of the population aged 15 and above was 0.01% and 0.002%, respectively [3]. The number of drug abusers annually admitted to detoxification centers in Riyadh, Jeddah, Dammam, and Qassim from 1996 through 2001 ranged from 4740 to 6650 patients with an average annual increment of 5.1% (unpublished data). Several studies were conducted in Saudi Arabia to describe the socio-demographic characteristics, pattern of substance abuse, and prevalence of blood-borne infections among drug abusers. For instance, 799 drug abusers from a voluntary detoxification unit in Jeddah were studied [4]. Sixty eight percent of subjects were under 35 years of age and 64% initiated drugs before age 25. Eighty seven percent used heroin or alcohol and 14% were dependent on more than one drug. Among heroin users, 91% injected the drug. The prevalence of hepatitis C virus infection among these patients was 69% [4]. In another study of 349 drug abusers in Jeddah, 281 (80.5%) subjects were intravenous drug users. The prevalence of HBsAg, anti-HBs, and anti-HBc was 12.6%, 49.0%, and 53.6%, respectively, suggesting that sharing of needles was a common practice [5]. In a more recent study in Jeddah including 1321 drug abusers, 1038 (78.6%) subjects were intravenous drug users and the prevalence of HBsAg and anti hepatitis D virus was 6.1% and 0.8%, respectively [6]. The prevalence of confirmed HIV infection among 2628 drug abusers in Jeddah, of whom 80% were intravenous drug users, was found to be only 0.15% [7]. Among 116 drug users in the Eastern province, 83% of subjects were below 32 years of age, 52.6% were unemployed, and the majority were of intermediate education [8]. Eighty-four percent of the patients abused heroin either alone or in combination with other drugs, 31% used alcohol, 26% used cannabis, and 10% used stimulants. The use of other drugs was rare [8].]

Sixth paragraph: Various forms of safe sex promotion and needle and syringe distribution have been supported in several countries with predominantly Islamic populations, including Bangladesh and Indonesia. There is a considerable body of scientific literature indicating that these programs do not encourage extra-marital sex or drug injecting, but that they do reduce the risk of HIV transmission in individuals and communities at risk of HIV.

Authors’ response

The studies that showed that these programs do not encourage extra-marital sex or drug injecting, but that they do reduce the risk of HIV transmission in
individuals and communities at risk of HIV were conducted in non-Muslim communities where the religious values may not be adhered to and respected as in Islamic communities. It should also be noted that HIV preventive strategies in some Islamic countries do not necessarily abide by the Islamic doctrine and that knowledge, attitude, and practice of Muslims in various Islamic societies do not necessarily conform to Islamic norms. Unlike the situation in some other Islamic countries, Islam in Saudi Arabia is strongly followed and adopted as a way of living and ruling. Therefore, the results of studies done outside Saudi Arabia and other similar countries such as Egypt and Malaysia may not necessarily be applicable to these religious countries.

Paragraph 6, last sentence was rephrased as follows: [Needle Exchange Programs, likewise, is viewed by Islam as a way of encouraging people engaged in intravenous drug use to continue this prohibited practice.]

Eighth paragraph (p 13): Do the authors have evidence that men with more than one wife are less likely to have extra-marital sex than those with one wife?

Authors’ response
This paper is meant to discuss some of the Islamic rules and concepts that are essential to preserve the well-being of societies and to protect communities from sexually transmitted infections as viewed by Muslims. These rules and concepts are undisputable as they come from God. Even though, Muslims do not seek evidence for the benefits of any order from our God who knows best, the benefits of the Islamic doctrine are so obvious to the followers of Islam. The paper is meant to explore and explain some of these Islamic values to non-Muslim communities in order to better understand the Muslims’ beliefs and practice.

The use of the term "provocation of men" in the same paragraph seems to suggest that men are somehow the victims and are unable to make informed choices that protect their health and that of their sexual partners.

Authors’ response
The words [to prevent provocation of men] were omitted.

Reviewer 2: Jack DeHovitz

Define bisexual contacts
Authors’ response
A new legend (legend a) for table 1 was added to define bisexual contact as follows [Defined as men who have sex with men and women].

Provide further elaboration of country of origin of expatriates
Authors’ response
A new paragraph (paragraph 2) was added to the Results section as follows: [Among 4761 HIV-infected expatriates, 3771 (79.2%) patients were from African countries, 624 (13.1%) patients, from Asian countries, 352 (7.4%) patients, from Middle East countries, and 14 (0.3%) patients, from Western countries. Ninety two percent of patients were from 10 countries, namely, Ethiopia (2214 patients or 46.5%), Nigeria (343 patients or 7.2%), Chad (329 patients or 6.9%), Yemen (309 patients or 6.5%), Sudan (267 patients or 5.6%), Eritrea (248 patients or 5.2%), India (219 patients or
4.6%), Somalia (176 patients or 3.7%), Pakistan (152 patients or 3.2%), and Bangladesh (133 patients or 2.8%), and the remaining 371 (7.8%) patients were from 41 other countries.

**Article would be strengthened by brief description of injection drug use issues - what is primary drug of use?**

Authors’ response

A new paragraph (paragraph 4) and 6 new references were added to the Discussion section as follows: 

Substance abuse is an increasing problem in Saudi Arabia as it is in the rest of the world [3]. Substances abused include injectable drugs such as heroin and cocaine and non injectable drugs such as cannabis and amphetamine-type stimulants. The estimated annual prevalence of heroin and amphetamine abuse in Saudi Arabia in 2000 as percentage of the population aged 15 and above was 0.01% and 0.002%, respectively [3]. The number of drug abusers annually admitted to detoxification centers in Riyadh, Jeddah, Dammam, and Qassim from 1996 through 2001 ranged from 4740 to 6650 patients with an average annual increment of 5.1% (unpublished data). Several studies were conducted in Saudi Arabia to describe the socio-demographic characteristics, pattern of substance abuse, and prevalence of blood-borne infections among drug abusers. For instance, 799 drug abusers from a voluntary detoxification unit in Jeddah were studied [4]. Sixty eight percent of subjects were under 35 years of age and 64% initiated drugs before age 25. Eighty seven percent used heroin or alcohol and 14% were dependent on more than one drug. Among heroin users, 91% injected the drug. The prevalence of hepatitis C virus infection among these patients was 69% [4]. In another study of 349 drug abusers in Jeddah, 281 (80.5%) subjects were intravenous drug users. The prevalence of HBsAg, anti-HBs, and anti-HBc was 12.6%, 49.0%, and 53.6%, respectively, suggesting that sharing of needles was a common practice [5]. In a more recent study in Jeddah including 1321 drug abusers, 1038 (78.6%) subjects were intravenous drug users and the prevalence of HBsAg and anti hepatitis D virus was 6.1% and 0.8%, respectively [6]. The prevalence of confirmed HIV infection among 2628 drug abusers in Jeddah, of whom 80% were intravenous drug users, was found to be only 0.15% [7]. Among 116 drug users in the Eastern province, 83% of subjects were below 32 years of age, 52.6% were unemployed, and the majority were of intermediate education [8]. Eighty-four percent of the patients abused heroin either alone or in combination with other drugs, 31% used alcohol, 26% used cannabis, and 10% used stimulants. The use of other drugs was rare [8].

**Screening of HIV infection needs clearer description. are all prisoners, STD patients, patients with TB, etc and expatriates tested?**

Authors’ response:

The word “all” was added in “Patients and Methods, paragraph 1, line 4” as follows “HIV cases are detected by HIV testing for various indications including clinical suspicion, screening of contacts of HIV-infected patients, routine screening of blood and organ donors, and testing of all prisoners, intravenous drug users, patients with other sexually transmitted infections, and expatriates pre-employment”.
4th paragraph in discussion is unnecessary, and does not add additional information or interpretation.
Authors’ response
As advised, this paragraph and the corresponding 10 references were omitted.

Table 2 is unnecessary - text is sufficient.
Authors’ response
Since this is the first official publication on HIV in Saudi Arabia and in view of lack of any other scientific papers on this subject from this country, we strongly feel that this table provides very important information which will be of particular interest to both health care workers and the public in Saudi Arabia.

Figure 2 is unnecessary, text is sufficient.
Authors’ response
We feel this figure is important to illustrate diagrammatically the declining trend of transfusion-transmitted HIV in Saudi Arabia. We therefore wish to keep it if Dr Jack DeHovitz won’t mind, otherwise, we will be ready to omit it.

Islamic means of prevention include permit for adolescent marriage, or allowance for up to 4 wives. Is there any data suggesting reduction in STD's with these allowances?
Authors’ response
There are no scientific studies either locally or internationally to confirm the effectiveness of these particular practices in reducing HIV transmission. However, it is conceivable that these practices are indeed effective means to prevent non-marital sex which is the main cause of sexually transmitted infections worldwide. A new paragraph (paragraph 9) and 3 references (9-11) were added to the Discussion section to generally address this question as follows: [Unfortunately, there is little published data on the effectiveness of the Islamic preventive strategies in reducing HIV transmission in Muslim communities. According to the United Nations and the World Health Organization data on HIV prevalence in different countries, however, the prevalence of HIV infection in Islamic countries is strikingly low compared to other countries [8,9]. A recent study showed that among 38 sub-Saharan African countries, the percentage of Muslims within countries negatively predicted HIV prevalence [10]. A survey of published journal articles containing data on HIV prevalence and religious affiliation showed that six of seven such studies indicated a negative relationship between HIV prevalence and being Muslim [10]].

Is there any data suggesting strategies to prevent HIV infection in Islamic countries have reduced incidence of HIV, other STDs, or HCV?
Authors’ response
As mentioned above in the response to the previous question the new paragraph (paragraph 9) and 3 references (9-11) that were added to the Discussion section to address the previous question addresses this question as well [Unfortunately, there is little published data on the effectiveness of the Islamic preventive strategies in reducing HIV transmission in Muslim communities. According to the United Nations and the World Health Organization data on HIV prevalence in different countries, however, the prevalence of HIV infection in Islamic countries is strikingly low compared to other countries [8,9]. A recent study showed that among 38 sub-Saharan African countries, the percentage of Muslims within countries negatively predicted HIV prevalence [10]].
HIV prevalence [10]. A survey of published journal articles containing data on HIV prevalence and religious affiliation showed that six of seven such studies indicated a negative relationship between HIV prevalence and being Muslim [10].

The Editor’s comment
Could you also please enclose a brief clarification as to why the title requires the inclusion of the phrase “from Islamic perspective”, other than that the study was performed in Saudi Arabia.

Authors’ response
The strategy to prevent HIV transmission in Saudi Arabia has been based on Islamic rules and values. This strategy has proven to be effective in keeping the prevalence of HIV at bay in this country. Since this is the first official publication on HIV from Saudi Arabia, we thought it would be important to discuss this strategy in some detail and to include a notion in the title to that effect to make the reader aware that this point is covered in detail in the article.

Other changes made:
Title
[Epidemiology of the human immunodeficiency virus in Saudi Arabia; 18-year surveillance results and prevention from Islamic perspective.] changed to
[Epidemiology of the human immunodeficiency virus in Saudi Arabia; 18-year surveillance results and prevention from an Islamic perspective.]

Results
Paragraph 3: the sentence [Approximately, one third of cases were identified because of clinical suspicion and the rest were identified in asymptomatic patients following HIV screening for the indications mentioned in table 3.] was changed to [Approximately, one third of cases were identified because of clinical suspicion and the rest of cases were asymptomatic subjects identified following HIV screening for the indications mentioned in table 3.]

Discussion
Paragraph 6: the word preventive was added in line 1 as follows [Some of the preventive strategies that are advocated and used in other non-Islamic countries such as “Safe Sex” and “Needle Exchange Programs” contradict the Islamic rules and values and as such can not be used as valid and acceptable strategies to prevent the spread of this infection in Islamic countries.]

Finally, we hope that the revised manuscript meet the expectations of yourself and the respected reviewers to be accepted for publication in BMC Infectious Diseases.

Thank you very much

Yours truly,

Corresponding author

Tariq A. Madani