Author's response to reviews

Title: Hospital-based HIV/HSV-2 seroprevalence among male patients with anal disease in Korea: cross sectional study

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Version: 2 Date: 30 August 2013

Dear Dr. Yuhua Ruan and Nicholas J. Van Wagoner

I appreciate for your precious revision comments and kind suggestion. I corrected the manuscript according to reviewer’s comments as following.

Reviewer’s report 1.
Title: Hospital-based HIV/HSV-2 seroprevalence among male patients with anal diseases in Korea
Version: 1 Date: 17 May 2013
Reviewer: Yuhua Ruan

Reviewer’s report:
This study investigated the characteristics of HIV and HSV-2 seroprevalence in male patients with colorectal diseases, and compared HIV seroprevalence among different age groups of all male patients with anal disease who were treated at S Colorectal Hospital between 2001 and 2011. The study results showed the HIV seroprevalence of male patients with anal disease was significant higher than that of in other disease fields. This scientific data can be used for prevention of HIV transmission.

Comments:
1. HIV infection was the highest in the group aged 10-19 years. The group aged 10-15 years or 10-16 years may have no sexual practice. The authors should explain why this age group has high HIV infection and/or class the group as ears or 16-19 years.

Thank you for your comments. We have reflected your comments in Discussion part of revised manuscript, page 11,12, lines 203-219.

For specific identification of high HIV seroprevalence in the group aged <20
years, we divided into groups aged <10 years, 10–14 years and 15–19 years. From 2001 to 2011, 1,061 male patients aged 15–19 years were treated and underwent HIV testing at the hospital. Ten HIV infections were found in the group aged 15–19 years.

A survey of male sexual behavior in Korea showed that sexual activity began around age 16 years [Ref: KCDC, The report of International AIDS symposium, 2004, The social and economic impacts of HIV/AIDS infection in Korea], and only 10–20% used condoms [Ref: Adolescents’s sexuality and school-based sex education in South Korea. Journal of Society for Health Education and Promotion, 2000, 19(4):45-60]. A survey of homosexual behavior in Korea showed that 60% of participants had a homosexual feeling before age 18 years [Ref: Sexual behavioral characteristics and the knowledge of HIV/AIDS among men who have sex with men in Republic of Korea. J Prev Med Public Health 2004;37(3):220-224.]. It is expected that the group aged 15–19 years is a group at high risk for STI.

2. Table 2, due to number of HIV infection among male patients with anal disease, 2009 was 10, the HIV data can be not included in this table 2.

Table1 shows that 20 HIV cases were found among the total number of 26,173 HIV-tested male patients with anal disease in 2009. Table 2 presents HIV and HSV-2 data; 2,038 samples randomly selected from 26,173 male patients tested for HIV in 2009 were subjected to HSV-2 testing. To avoid confusion, we corrected the Methods and Table 2 as follows.


[Table 2] of revised paper: we corrected the footnote (line 13) and changed the position of ‘Total’ in Table 2.

# footnote (line 22): The 2,038 HSV-2 samples randomly selected among 26,173 male patients with anal disease tested for HIV in 2009.

# the ‘Total’ position is moved from the bottom to the top in the Table 2.

Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Needs some language corrections before being published Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: ‘I declare that I have no competing interests’
Reviewer’s report 2.

Title: Hospital-based HIV/HSV-2 seroprevalence among male patients with anal diseases in Korea

Version: 1 Date: 22 May 2013
Reviewer: Nicholas J. Van Wagoner

Reviewer's report:
In the manuscript entitled, “Hospital-based HIV/HSV-2 seroprevalence among
male patients with anal diseases in Korea" the author present epidemiological finding for both HIV and HSV-2 in their colorectal hospital. They make the case that diagnostic rates are higher among patients presenting with anal disease than in patients presenting with non anal diseases. Thus targeting men presenting with anal disease for HIV screening could increase HIV diagnoses.

Major Compulsory Revisions

1. English grammar is incorrect throughout the manuscript making the manuscript a challenge to read. I would advise finding a good copy editor to ensure accuracy not only in grammar but also to ensure that accuracy of meaning is also conveyed to the reader.

The revised manuscript has been checked by a professional English editing company by Edanz (www.edanzediting.com/bmc1).

2. Background: I would suggest working to establish your rationale more clearly. Why would men with anal disease be more likely to have HIV. Is it related to sexual practices among men who have sex with men? Is there another reason?

We described the sexual association between HIV infection and anal disease in Korea and other studies in the Background section of the original manuscript (lines 62–70).

(lines 62-70: The ratio of males to females among reported HIV cases is approximately 11:1. ~ of the HIV-infected population has anal disorders, which are also the most frequent cause for surgery in this group (4, 5).)

And we added another report in the revised manuscript of background, page 4, line 71-73)

Among men who have sex with men attending a sexually transmitted infection (STI) clinic, 30.8% had dysuria, pus, and urethral ulceration, and 37.1% had pus, bleeding, ulceration, and/or pain in the rectum [PLoS One 2013 Apr 25;8(4):e59072].

There might have been more men who have sex with men with anal diseases among the patients who visited the colorectal hospital than other hospitals.

As well, the purpose for presenting data on HSV-2 is unclear to me.

We have reflected your comments in background part of revised manuscript, page 5, lines 78-82, as follows.

Genital ulcers have been associated with increased risk factors for HIV infection, and genital herpes is usually caused by herpes simplex virus (HSV)-2 [MMWR 2002:51(No. RR-6)]. Our previous study had compared HSV-2 seroprevalence in HIV-infected males with that in the general male population in Korea, which was two or three times higher among HIV-infected males. [J Korean Med Sci 2007;22:957–62].

We wanted to identify the status of HSV-2 seroprevalence among male patients
with anal disease, which was higher than the HIV seroprevalence among the general male population.

3. Methods: It is unclear to why you chose to stratify by age groups. Please make this clear.

We have reflected your comments in background part of revised manuscript, page 5, lines 82-84.


It is important that HIV seroprevalence is characterized by the age specific trait reflected sexual activities because 99% HIV cases infected by sexual contacts in Korea.

That is why we wanted to establish the HIV and HSV-2 seroprevalence in different age groups among male patients with anal diseases.

4. Methods: Statistical Analysis: You included under intestinal disorders hemorrhoids, anal fissure and anal fistula. What about perianal condyloma and squamous cell carcinoma of the rectum? Were this included? If not why not since both are associated with receptive anal sex. What disorders were included in the control group?

That is good points. We treated male patients with all kinds of anal disease in this study. We corrected the Methods in the revised manuscript, page 7, line 121.

Patients suffering from general anal diseases including hemorrhoids, anal fissure and anal fistula were grouped as anal disease patients, and patients who visited the hospital for a health checkup or for another intestinal disorder were categorized as nonanal disease patients.

Patients with any type of anal disease were grouped together as the anal disease patients, and patients who visited the hospital for a health checkup or for another intestinal disorder were categorized as the nonanal disease patients.

Also, what cut off did you use for Herpe Select seropositivity?

The assay used for detection of HSV type 2 IgG antibody was the FDA-approved type-specific, glycoprotein G-based (gG-2) product, HerpeSelect (Focus Diagnostics, Cypress, CA). This enzyme immunoassay uses a spectrophotometer to measure the color change associated with the presence of HSV-2 antibodies which is quantified by an optical density. The index value is calculated by dividing the specimen optical density by the mean of the cutoff calibration absorbance values. Index values for samples that read above the absorbance limit of the spectrophotometer as >1.1 are positive.

We have reflected your comments in method part of revised manuscript, page 7,
HSV-2 results were reported as an index value relative to the cut-off calibrator. An index value >1.10 was presumptive for the presence of IgG antibodies to HSV-2.

5. Line 117: I suspect you are missing "non" before anal disease.

To avoid confusion, we corrected method part of revised manuscript, page 7, line 127.

Line 117: HIV seroprevalence in different age groups of patients with anal disease and HSV-2 seroprevalence in different age groups of patients with anal disease, with a 95% confidence interval.

# HIV and HSV-2 seroprevalence in different age groups of patients with anal disease, with a 95% confidence level.


The trend of HIV seroprevalence over time did not show any specific pattern in any of the age groups.

We have reflected your comments in results part of revised manuscript, page 8, lines 143-144.

The trend in HIV seroprevalence over time did not show any specific pattern in any of the age groups: under 20 (P=0.5982), 20–29 (P=0.3675), 30–39 (P=0.7476), 40–49 (P=0.1336), 50–59 (P=0.0815), and #60 (P=0.3709) years.

7. Results: I believe that it is an important finding that younger men 10-19 had the greatest likelihood of HIV diagnosis. This warrants further focus in the discussion.

I agree with your opinion. Thank you for your kind suggestion. We have reflected your comments in discussion part of revised manuscript, pages 11-12, lines 203-219.

For specific identification of high HIV seroprevalence in the group aged <20 years, we divided into groups aged <10 years, 10–14 years and 15–19 years. From 2001 to 2011, 1,061 male patients aged 15–19 years were treated and underwent HIV testing at the hospital. Ten HIV infections were found in the group aged 15–19 years.

A survey of male sexual behavior in Korea showed that sexual activity began around age 16 years [Ref: KCDC, The report of International AIDS symposium, 2004, The social and economic impacts of HIV/AIDS infection in Korea], and only 10–20% used condoms [Ref: Adolescents’s sexuality and school-based sex education in South Korea. Journal of Society for Health Education and Promotion, 2000, 19(4):45-60]. A survey of homosexual behavior in Korea showed that 60% of participants had a homosexual feeling before age 18 years.
[Ref: Sexual behavioral characteristics and the knowledge of HIV/AIDS among men who have sex with men in Republic of Korea. J Prev Med Public Health 2004;37(3):220-224.]. It is expected that the group aged 15–19 years is a group at high risk for STI.

8. Results: Lines 150-151. My interpretation of this is that only 1 patient was coinfected with HIV and HSV-2. If this is the case, why would the epidemiology be different in Korea than else where?

Lines 150-151: The infection with HIV and HSV-2 was found in only one patient (4/10,000) of the total number tested, who was in his thirties.

Five men were diagnosed with HIV, three of whom were in their 20s, and one each aged 30–39 and 40–49 years. HSV-2 seroprevalence increased with age (P<0.0001). There were a few cases of HIV/HSV-2 co-infection among male patients with anal disease in Korea.

9. Discussion: The case is made for a strong association between anal disease and HIV infection in men presenting to the colorectal hospital. It would greatly strengthen the manuscript if you had behavioral correlates. If you captured sexual behavior (i.e. sex with women or sex with men) or specific sex acts and could correlate with your findings, the manuscript would be stronger.

Alternatively, if stigma associated with same sex sexual behavior is high and most men are unlikely to tell their health care providers about their sexual orientation, then screening in the facility offers a way to improve yield.

That is good points. We agree that lack of data on sexual behavior is a major limitation of our study.

When we designed this study, we formulated a questionnaire survey including sexual risk behavior. However, most of the participants refused to answer it.

Forty-three percent of HIV-infected Koreans were reported to be infected from homosexual contact. The proportion of men among HIV-infected individuals has increased annually in Korea. The data related to homosexual activity among those with HIV infection might have been underestimated because of the stigma surrounding homosexuality in Korea.

10. Discussion: Lines 193-195. I would show this data.

Line 193-195: A high proportion of HIV-infected individuals in this study contracted the virus through homosexual contact.

Approximately 70% of HIV-infected male patients in the colorectal hospital in 2007–2011 were reported to be infected by homosexual contact. However, this might have been an underestimate, owing to the stigma of homosexuality in Korea.

We have reflected your comments in methods, results and discussion part of revised manuscript as follows.
[Discussion] of revised paper (page 12, lines 220-222): Approximately 70% of HIV-infected individuals in the present study contracted the virus through homosexual contact, according to the HIV database of KCDC.

11. Discussion Lines 201-204: Review for clarity. Are you saying that there are specific lesions associated with HIV or that HIV prevalence is higher in men presenting with certain complaints?

Lines 201-204: Therefore, this study shows that ensuring that colorectal surgeons can easily identify lesions associated with HIV infection in male patients with anal disease to prevent a misdiagnosis or delayed diagnosis is critical to stopping the spread of HIV.

As is generally known, HIV-infected individuals often suffer from common anal disorders such as fistula and fissure as well as various STDs including condyloma acuminate. However, what we are meaning is not that there are particular anal lesions related to HIV-infection.

Rather, it is that, considering that HIV prevalence is high among male patients who visit colorectal hospital for anal disorders, stronger efforts are needed to enhance HIV testing for this group.

12. Discussion Lines 211-214: Why is seroprevalence so much lower in this Korean Population?

Lines 211-214: In this study, about 20% of HIV-infected individuals were found to have HSV-2. Moreover, HSV-2 seroprevalence in male patients with anal disease was similar to that in the general male population.

That is good points. I agree your comment that HSV-2 seroprevalence was too lower in this study. And answers to the reviewer’s comments were added in Discussion part, page 14, lines 250-255.

Finally, we don’t have data on sexual behavior to find out the reason of high HIV seroprevalence among male patients with anal disease. And, HSV-2 seroprevalence was low in male patients with anal disease, which differed from other studies [Sex Transm Dis. 2012 Feb;39(2):154-60., Sex Transm Dis 2009; 36:165-169]. It will be necessary to establish the relationship between the study results and the epidemiological characteristics of the study subjects in Korea.

13. In its current state, I do not understand the purpose for including data related to HSV-2. A stronger case for its inclusions needs to be made.

As already stated in answer comment #2, there are many studies of HIV and HSV-2 related to sexually transmitted infections. Therefore, we wanted to establish HSV-2 seroprevalence in male patients with anal disease, who have a reported higher frequency of HIV than any other group of male patients. We expected a higher HSV-2 seroprevalence in male patients with anal disease. Contrary to our expectations, HSV-2 seroprevalence was low in male patients with anal disease, which differed from the results of other studies.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests.

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I would like to add one more author who contributed to the important part of the data analysis in the manuscript with agreement by all authors of the article.
Here is the author’s information
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We look forward to receiving great news and thank you for your interest in my article.
Best regards
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