



**SDI Review Form 1.6**

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| Journal Name:            | <a href="#">International Journal of TROPICAL DISEASE &amp; Health</a>     |
| Manuscript Number:       | Ms_IJTDH_24342                                                             |
| Title of the Manuscript: | Helicobacter pylori infection as a risk factor for coronary artery disease |
| Type of the Article      | Original research Article                                                  |

**General guideline for Peer Review process:**

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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**PART 1: Review Comments**

|                                     | Reviewer's comment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
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| <b>Compulsory</b> REVISION comments | <ol style="list-style-type: none"> <li><b>Title</b> of the study is misleading. The authors didn't follow patients with <i>H. pylori</i> infection and the risk/development of coronary artery disease.</li> <li><b>Aim:</b> after reading the results and discussion the study is not in concordance with the aim. Also the title is not compatible with the aim. Further, it is written in the aim "to evaluate association between <i>H. pylori</i> infection and other risk factors in suspected CAD patients". What do authors mean by "suspected", namely under Study Subjects they define two groups and the study group are patients with manifest CAD ("history of coronary artery bypass graft surgery, a history of myocardial infarction...").</li> <li><b>Participants:</b> it is not clear how the study groups were recruited? There seems to be a huge selection bias. Were these consecutive patients with dyspeptic symptoms? What is meant by "The presence or absence of symptoms suggestive of CAD..."? Did all subjects undergo electrocardiogram (ECG), echocardiography, ECG stress test or coronary angiography? How is it possible that control subjects had the same risk factors as patients with manifest coronary artery disease? Where were the control subjects selected from? What is the prevalence of arterial hypertension in KSA in a population of mean age of 32.6 years? 55% seems a lot. A study of Al-</li> </ol> | <p>Thank you very much for your valuable comments</p> <ol style="list-style-type: none"> <li>Title match with results that the prevalence of seropositivity for <i>H. pylori</i> was higher in patients compared to controls (47{78.3%} versus 33 {55%} P&lt;0.05).</li> <li>The aim of this prospective study was to evaluate <i>H. pylori</i> infection as risk factor in CAD patients and to investigate the influence of <i>H. pylori</i> infection on cardiovascular risk factors (lipid profile and hs CRP levels).</li> </ol> <p>Suspected removed</p> <ol style="list-style-type: none"> <li>yes these all consecutive patients presented with dyspeptic symptoms the presence of symptoms suggestive of CAD; such as exertional chest pain or dyspnea.</li> </ol> <p>control subjects were selected according to clinical examination and ECG who attended GIT clinic with dyspepsia</p> <p>most of the control population were aged more 40 years old</p> |



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|  | <p>Nozha and co-workers report significantly lower prevalence (1).<br/>Al-Nozha MM, Ali MS, Osman AK. Arterial hypertension in Saudi Arabia. Ann Saudi Med. 1997 Mar;17(2):170-4.</p> <p>4. What does it mean: "Patients on drug therapy known to alter lipid indices (e.g. <math>\beta</math>-blockers, OC pills), and Patients receiving antihyperlipidemic therapy." The sentence is not complete. Were patients taking statins excluded? Statins are the mainstay therapy of patients with CAD.</p> <p>5. How was <b>the sample size</b> of the study population defined?</p> <p>6. <b>Methods: H. pylori IgG ELISA test:</b> it seems the text was just copied from the instructions: "Take a new reading at 405 nm the O.D. are higher than 2.000." What was done with the doubtful results and how many results were doubtful? The authors should describe that in detail.</p> <p>7. <b>Results:</b> The group of patients with CAD was very young (<math>37.8 \pm 15</math> years), what is meant by range 16 – 80? This is at least 20 years younger cohort than usual study cohort of coronary artery disease patients.</p> <p>There is a discrepancy of the reported results in Table 2 and the abstract: "H. pylori was confirmed in 90 (75 %) of total 120 patients..." whereas in Table 2 it is written that 75 (62.5%) of positive results were confirmed by serology.</p> <p>What were the values of laboratory markers in control subjects? Only data of laboratory markers in the study group regarding the H. pylori infection is presented, how can the authors make any conclusions if they don't compare the results with the control group?</p> <p><b>Discussion:</b> at least half of the discussion is about the results of the endoscopic investigations, but no</p> | <p>4. Exclusion criteria were: prior <i>H. pylori</i> eradication therapy, consumption of acid-suppressive drugs or antibiotics in the preceding 1 month, history of vagotomy or operations on the upper gastrointestinal tract, known history of gastrointestinal pathology and patients on drug therapy known to alter lipid indices (e.g. <math>\beta</math>-blockers, OC pills), and Patients receiving anti-hyperlipidemic therapy. All cardiac selected were stable with only mild CAD so treatment stop</p> <p>5. <b>the sample size</b> of the study population defined by agreement between authors and restricted by the study duration</p> <p>6. <b>methods:</b> the doubtful results were 2 only and we asked for other new samples (we have very well validated automated machine ).</p> <p>7. Results:<br/>The patients aged 16 to 35 years old were only 2 patients and most of the patients with CAD were aged more than 35 years old while 75 (62.5%) was detected by serology. there was a typing error and corrected</p> <p>according to the aim of the study The aim of this prospective study was to evaluate <i>H. pylori</i> infection as risk factors and to investigate the influence of <i>H. pylori</i> infection on cardiovascular risk factors (lipid profile and hs</p> |
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|  | <p>association/relevance to coronary artery disease is presented.</p> <p>The authors compare their results to the study of Mendall and co-workers, however the cited manuscript by Mendall is describing the infection with Chlamydia pneumoniae.</p> <p><b>8. Conclusions:</b> should be a general interpretation of the results. Further, they should answer the aim of the study. The conclusions of this study don't answer the aim. Authors shouldn't report the values in the conclusions.</p> <p><b>9. Ethical Issues:</b> It is not clear why the authors wrote that the "Ethical approval is not applicable". The study involves control subjects, who don't need endoscopy, so they should be informed why they undergo endoscopy, what the risks and benefits are. Endoscopy is an invasive examination and the study should be approved by ethics committee as well as all subjects should be informed about the study in order to give their informed consent.</p> | <p>CRP levels) among CAD patients</p> <p>Frank et al., 2014 [24] not Mendall</p> <p><b>8. Conclusion</b></p> <p><i>H. pylori</i> infection increases the risk of CAD, and should be considered as a risk factor for CAD, also there was significant association between <i>H. pylori</i> infection and increased triglyceride hsCRP levels and decreased HDL-c. Further, prospective large trial is needed to confirm our finding.</p> <p>The control group already informed before endoscopy as they were complaining of dyspepsia</p> <p><b>9. Ethical approval</b></p> <p>Ethical clearance was obtained from the hospital's ethics committee.</p> <p>There was some confusion regarding this point</p> |
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| <p><b><u>Minor</u></b> REVISION comments</p>   | <p><b>The English</b> needs improvement, it should be edited by a native-English speaking professional.</p> <p>The use of <b>abbreviations</b> is confusing throughout the article. Authors use the abbreviations CAD and CHD, without stating what they mean. There are several other abbreviations that are not defined in the text, e.g. all laboratory parameters: hsCRP, TC, TG,... , OC pill, GERD and UGI.</p> <p><b>References:</b> the order of the references doesn't suit the citations in the text of the manuscript. Further, the references are not cited correctly: e.g. ref. 26 was not published in Infect. Dis. but in The Journal of Infection.</p> <p><b>Tables:</b> Table 3 should be Table 1, describing the basic characteristics of the study groups.</p> | <p><b>coronary artery disease (CAD)</b><br/>Total cholesterol (TC), high density lipoprotein cholesterol (HDL- c) and triglycerides (TG) THESE written in abstract</p> <p><b>oral contraceptive pills</b></p> <p><b>gastroesophageal reflux diseases (GERD)</b></p> <p>Highly sensitive C-reactive protein (hs CRP)</p> <p><b>References revised</b></p> |
| <p><b><u>Optional/General</u></b> comments</p> | <p>This is an interesting study because the association between H. pylori infection and cardiovascular risk is still under investigation and findings could be of great importance. However, the study has several inconsistencies and flaws, which would need to be significantly improved in order to publish the manuscript.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                          |