

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 40962

Title: Serum anti-Helicobacter pylori antibody titer and its association with gastric nodularity, atrophy, and age: A cross-sectional study

Reviewer's code: 01557050

Reviewer's country: Japan

Science editor: Ruo-Yu Ma

Date sent for review: 2018-07-17

Date reviewed: 2018-07-24

Review time: 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dr. Toyoshima, et al investigated 'Serum anti-Helicobacter pylori antibody titer and its association with gastric nodularity, atrophy, and age: A cross-sectional study'. The manuscript is informative and well-presented. The reviewer has no comments.



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INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 40962

Title: Serum anti-Helicobacter pylori antibody titer and its association with gastric nodularity, atrophy, and age: A cross-sectional study

Reviewer's code: 01552044

Reviewer's country: Italy

Science editor: Ruo-Yu Ma

Date sent for review: 2018-07-17

Date reviewed: 2018-07-24

Review time: 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The Authors describe an interesting association between anti-H. pylori antibody serum titers and specific endoscopic findings in a large series of patients. The manuscript is interesting, well written, with conclusions supported by results



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 40962

Title: Serum anti-Helicobacter pylori antibody titer and its association with gastric nodularity, atrophy, and age: A cross-sectional study

Reviewer's code: 02954019

Reviewer's country: Japan

Science editor: Ruo-Yu Ma

Date sent for review: 2018-07-17

Date reviewed: 2018-07-28

Review time: 11 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting and attractive manuscript describing the association between H. pylori antibody titer and 1) clinical characteristics and 2) endoscopic findings based on Kyoto classification. They concluded that nodularity, atrophy, and age 40–59 years

(versus age ≥ 60 years) were correlated with a high serum antibody titer in H. pylori-infected patients in multivariate analysis. They also demonstrated that intestinal metaplasia and atrophy were related to age ≥ 60 years in group C. However, several concerns are listed below. The meaning of negative H. pylori serology is not simple. Group A (H. pylori antibody titer $<3\text{U/ml}$) and Group B ($3\text{--}9.9\text{U/ml}$) include three subgroups of subjects; H. pylori uninfected case, infected cases and unintended eradicated cases. Group A and B include many H. pylori uninfected cases, and because high prevalence of FGP, RAC, reflux esophagitis in H. pylori negative cases have been already reported by many investigators, the reported association by authors seems to be of little significance. The significance of low positive H. pylori titer ($10\text{--}49.9$) is not also simple. This subgroup includes both of 1) low risk subjects with mild atrophy who are typically normal pepsinogen, and 2) high risk subjects with profound atrophy who are typically being atrophic pepsinogen. Thus, various endoscopic findings are consequently seen in subjects of Group A and C, and presentation of typical endoscopic findings is not necessarily important (Fig 1). Subjects with high titer of H. pylori seem to be a characteristic subgroup among H. pylori seropositive cases. What should we consider if high H. pylori antibody titer cases present in daily clinical practice? It seems to be an interesting question in daily clinical practice. Thus, I recommend analyzing only H. pylori positive cases, and then, the characteristics of high titer case should be investigated. I recommend considering to change Table 1. It may be better to include three subgroups; total, Group C and group D (or low positive titer group and high positive titer group). Multiple regression analysis should be done base on the results of comparison of high titer and low titer cases. Is it necessary to investigate the association between age >60 and endoscopic finding? The obtained results seem to be confusing. In Group C, $>60\text{y}$ is associated with atrophy and IM, which is understandable because progression of atrophy is considered to occur in aged subjects, and their

antibody titer spontaneously decreased by the profound atrophy. However, I can't understand the results that >60y subjects in Group D are associated with IM, but not atrophy. IM is generally seen in advanced stage of atrophy. How can you explain this finding? Based on the author's result, aged subjects (>60) with high titer of H. pylori serology show IM, but the antibody titer does not decrease despite the advanced atrophy. Is it right? Thus, I recommend deleting these results (Fig 4). Multivariate analysis also seems to be difficult in Group D because of the small sample size. The significance of high titer of H. pylori serology has been overlooked. Thus, I consider it important to investigate the association between high titer and endoscopic findings as describe in this manuscript. Because H. pylori antibody titer is an only method to predict the bacterial density of gastric mucosa, endoscopic findings with high H. pylori density are also clarified by this investigation, and may be useful.

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