



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 55216

**Title:** Latest Developments in Chronic Intestinal Pseudo-obstruction

**Reviewer's code:** 00043256

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** United Kingdom

**Author's Country/Territory:** China

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**Reviewer chosen by:** Jia-Ping Yan

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**Review time:** 1 Day and 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

Thank you for asking me to review this article. It is a summary of published work regarding Chronic Intestinal Pseudo-obstruction. The article is easy to read, a sensible discussion of the main clinical features of Chronic Intestinal Pseudo-obstruction, and provides a lengthy list of references for further reading. Although Chronic Intestinal Pseudo-obstruction is not common, to the interested professional (adult or paediatric surgeon, gastroenterologist), it could be a useful point of reference. I have a question and a comment for the authors. Question - in the introduction the authors state 'Most congenital cases are sporadic, and patients have no clear family history; however, the majority of patients with CIPO are autosomal dominant [12,13].' I was confused by this, as the 2 parts of the sentence seem to contradict each other. Could the authors clarify this please? Comment - at the end of the discussion the authors state 'Clinicians should improve their understanding of this disease because it is very important to diagnose and treat patients early, which improves patients' quality of life and their long-term prognosis.' Although I agree that clinicians should keep themselves educated, I could not see any reference in their paper that concluded that early diagnosis improved prognosis. I read reference 92 (Amiot et al, Am J Gastroenterol. 2009;104(5):1262-1270.) and I could not see that the data in this paper came to the conclusion that early diagnosis improves prognosis. However, I could be wrong and I look forward to the authors' comments.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 55216

**Title:** Latest Developments in Chronic Intestinal Pseudo-obstruction

**Reviewer's code:** 02276086

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** China

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**Reviewer chosen by:** Jia-Ping Yan

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

The authors review the diagnosis, pathogenesis, and treatment of CIPO with the goal of improving clinicians' understanding of this complex and poorly understood disease. The review is relatively brief, superficial, and lacking in details. My comments are detailed below.

1. The second sentence of the Introduction states that CIPO is caused by the enteric neuromusculature "and/or its autonomic innervation." This sentence needs to be clarified. The autonomic innervation of the gut includes both intrinsic and extrinsic innervation. The intrinsic part is the enteric nervous system, which is already included in the "enteric neuromusculature." Primary CIPO is due to a disorder of the enteric neurons, muscles, or ICCs. Are abnormalities of the extrinsic innervation of the gut known to cause CIPO?
2. It would be helpful to explain briefly the difference between primary and secondary CIPO, a distinction that is often made in the literature.
3. The "Classification & Etiology" section states that exposure to alcohol can lead to CIPO. Is there any evidence for this? The authors cite Reference #16, but that is an article about POLG mutations.
4. In their review of treatment options, the authors should include use of immunosuppressive therapy in carefully selected patients given the identification of an inflammatory or immune-mediated neuropathy or myopathy in some individuals with CIPO.
5. The incidence of CIPO in children is much higher than in adults. This is presumably because affected children do not survive to adulthood. If that is the reason, this should be clarified in the text.
6. The authors state that "the majority of patients with CIPO are autosomal dominant." This is not correct. They cite two references from the 1980s, one of which is a case report and the other is a case series. Most cases of CIPO do not run in families. Those that do can be inherited in autosomal dominant, autosomal recessive, or x-linked recessive fashion.
7. In the section on "Classification & Etiology," the text suggests that all cases of congenital CIPO include a history of toxic exposure, which is not true. Autoimmunity is another potential cause, possibly post-infectious



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etiologies also. The sentence should be changed to “The acquired pathogenesis of CIPO may include a history of...” 8. Mesenchymopathies refer to ICC abnormalities, but the authors include Reference #30 in this category. That study is about connective tissue development in the gut, desmosis, and intestinal dysmotility. Its relevance to CIPO is unclear. 9. The authors state that the age of onset of CIPO is a median of 17 years. That is based on Reference #31, which is a small study of 20 adult patients. The age of onset of the condition is usually much younger. 10. The section on diagnosis does not mention genetic testing at all. There are several genes associated with neuropathic and myopathic causes of CIPO and these should be discussed. 11. The authors refer to “CIPO patients with Hirschsprung’s disease.” This needs to be explained. Is this referring to patients with Hirschsprung disease prior to pullthrough surgery? After surgery? Those with total intestinal aganglionosis? 12. The term “uroschesis” is not defined. 13. The manuscript cites a 10-16% mortality rate for children with CIPO. In the “Prognosis” section it states that 10-25% of children with CIPO die before adulthood. These numbers should be reconciled.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 55216

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**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

The topic of manuscript is good and will be of interest to readers. There are a lot of grammatical and formatting mistakes. It should be read and corrected by someone proficient in English. Pathology, pathogenesis and differential diagnosis should be in more detail.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 55216

**Title:** Latest Developments in Chronic Intestinal Pseudo-obstruction

**Reviewer's code:** 00003629

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Emeritus Professor

**Reviewer's Country/Territory:** Greece

**Author's Country/Territory:** China

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

A. General Comments: 1. The article needs English language correction in several places. 2. A better description of the clinical picture and the mode of presentation of the disease is advised. 3. Authors should pay more attention in the differential diagnosis of CIPO.

B. Major Comments: 1. (Page 4, Line 16): Besides mentioning only frequency of symptomatology, authors should describe the actual clinical presentation of a CIPO patient, eg usual mode of presentation, preceding symptoms, quiescent intervals if any, acute symptoms, etc. 2. (Page 4, Line 20): What type of abdominal pain? Colicky? Persistent? Nocturnal? Postprandial? Generalized? Localized? 3. (Page 4, Line 21): This sentence needs further clarification. 4. (Page 4, Line 22): Do the authors imply that a symptom-free interval may last for several months? 1. (Page 4, Lines 25-26): How often the urinary symptoms precede the GI ones? How common are urinary tract infections in CIPO? Gall bladder dilatation? Cholelithiasis? 2. (Page 5, Line 1): Why the correct diagnosis of CIPO is so much delayed and its misdiagnosis so common? The authors must expend more on that point, either in this or in another section of their review. 3. (Page 5, Line 1-Diagnosis): A note of similarities, differences and possible coexistence between CIPO and Hirschsprung's disease should be made somewhere in the text. 4. (Page 6, Line 4): After mentioning all the pros and cons of the diagnostic methods in CIPO, what is the authors conclusion? How the diagnosis of CIPO can be established without any doubt? 5. (Page 8, Line 28): Authors should mention the use of prealbumin, as a marker of malnutrition, in the context of evidence described in the article *Am J Med* 2015;128:1023.e1-22. 6. (Page 10, Line 1): The authors refer to a "lifetime" or to "annual" morality rate?

C. Minor Comments: 1. (Page 3, Line 6): Do authors mean "1 per 40,000 births?" 2. (Page 3, Line 6): Consider changing the expression to "2.0-2.4 per 1,000,000". 3. (Page 3, line 21): Please give a reference. 4. (Page 5, Line 6): Plain upright abdominal radiography. 5. (Page 5, Line 12): "cine-MRI". 6. (Page 10, Line 13): Please replace the



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term “uroschesis” by “urinary retention” a term more familiar in western medical terminology.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 55216

**Title:** Latest Developments in Chronic Intestinal Pseudo-obstruction

**Reviewer's code:** 01429143

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Chief Doctor

**Reviewer's Country/Territory:** United Arab Emirates

**Author's Country/Territory:** China

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

I read with interest the review by Changzhen Zhu et al. about CIPO. The manuscript is well written and updated. I have just minor comments In the epidemiology section I suggest to mention data about the prevalence of the idiopathic against the the genetic and secondary cases of CIPO Regarding the diagnosis I do disagree about the role of manometry. Intestinal manometry can be useful to define the pathophysiological (neuromuscular) mechanisms involved in CIPO (e.g. neuropathy or myopathy), although it has a low diagnostic specificity. Intestinal manometry can differentiate mechanical from functional forms of sub-occlusion, provided that the organic cause is at the early stage. See i.e. Stanghellini V et al. Gut 1987, Fell JME et al Gut 1996, Cucchiara S et al. JPGN 1994.