Undergraduate Students, Medical, Biomedical and Health Sciences

A meta-review of meta-analyses and an updated meta-analysis on the efficacy of chloroquine and hydroxychloroquine in treating COVID19 infection

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Background

- Controversy surrounds the efficacy of the antimalarial drug chloroquine (CQ), and its derivative, hydroxychloroquine (HCQ), on their efficacy and possible harm when used for the treatment of COVID19.
- Findings from meta-analyses, and primary studies have produced conflicting findings on the efficacy and safety of these drugs.

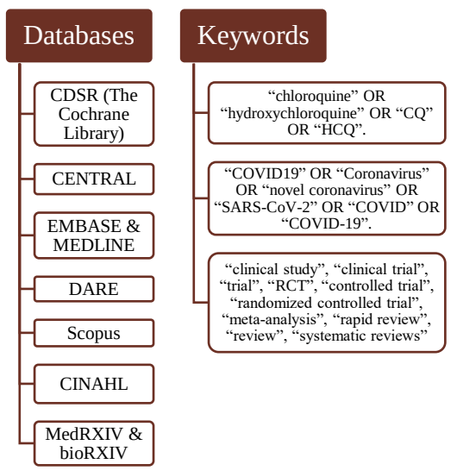
Aims & Objectives

- To synthesize the findings from systematic reviews and meta-analyses as well as to update the evidence using a meta analysis in evaluating the efficacy and safety of CQ and HCQ with or without Azithromycin for the treatment of COVID19 infection.

Methods

- A meta-review of published systematic reviews and updated meta-analysis of experimental studies where either HCQ or CQ with or without Azithromycin were used for the treatment of COVID19.

Search strategy:



Data extraction:

- For each study, two authors independently extracted data and assessed quality.

Quality Assessment:

- Risk of bias was assessed using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) tool for reviews and the MethodologicAl STandard for Epidemiological Research (MASTER) scale for the experimental studies.

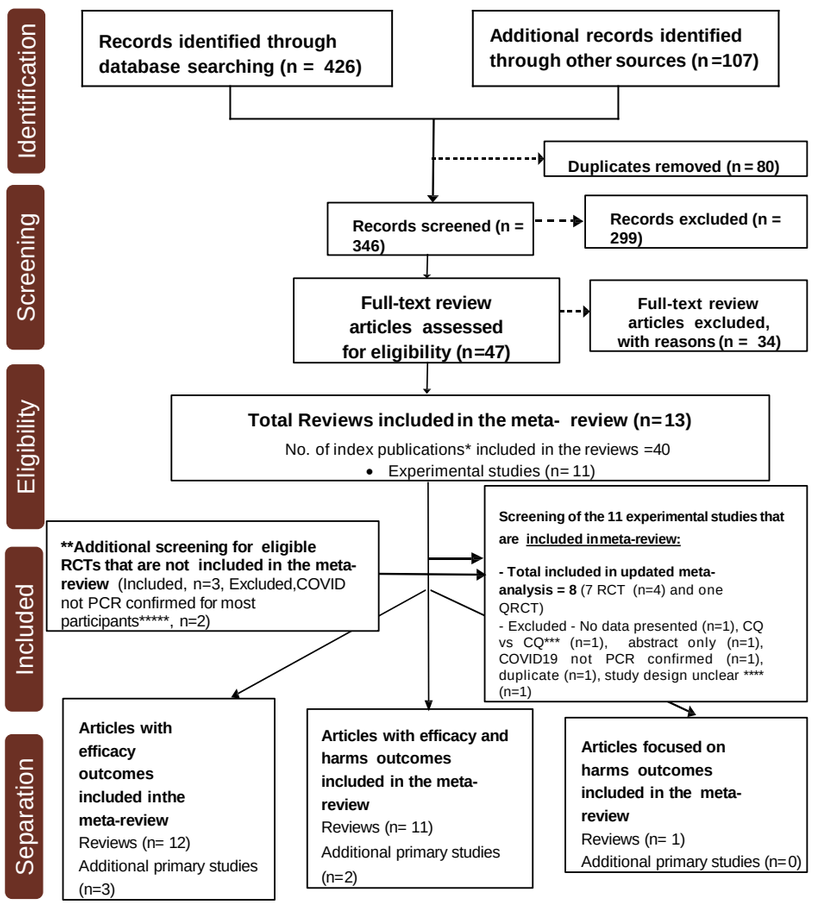
Outcomes:

- The main outcome for both the meta-review and the updated meta-analysis was mortality. Secondary outcomes were transfer to the intensive care unit (ICU) or mechanical ventilation, worsening of illness, viral clearance and the occurrence of adverse events.

Synthesis of findings:

- Synthesis of findings from different reviews was done using a combination of a structured summary of findings from the reviews and presentation in forest plots.
- For the updated met-analysis, findings from included experimental studies were synthesized using quality effect model.
- The Cochran Q test p-value was used to test for and the I^2 statistic to quantify heterogeneity.

Results



Index publication is the first occurrence of a primary publication in the included reviews. **Additional eligible primary studies that had not been initially identified by the search of the relevant reviews or obtained by updating the search of the included reviews. ***study compared high dose chloroquine against a low dose chloroquine. ** study design not clear as both groups received HCQ, ***** most participants in study diagnosed using symptoms and not PCR*

Figure 1. PRISMA chart for studies selection process

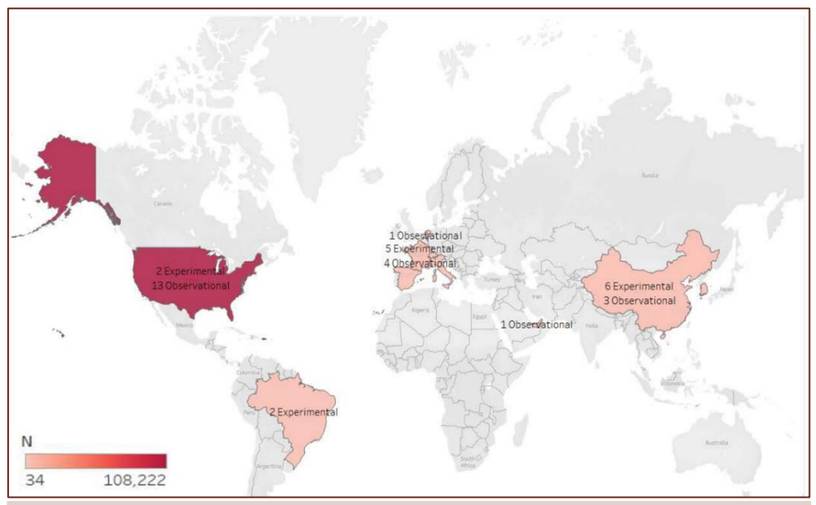


Figure 2. Location of all primary studies in the included reviews
N = sample size of the index study.
Labels on the map indicates number & type of studies within each country.

Meta-review of systematic reviews results

All-cause of mortality

Overall, all meta-analyses showed higher risk of mortality with HCQ with/without Azithromycin, compared to control (Fig 3).

Figure 3. Results from meta-analyses included assessing all-cause of mortality outcome.

ICU transfer and disease exacerbation

Most reviews found no significant differences between HCQ group and control, in the risk of transfer to ICU and disease exacerbation.

Virological cure and adverse events

Most meta-analyses found no significant differences between HCQ group and control, in virological cure but significantly higher risk of adverse events for HCQ (Fig 4).

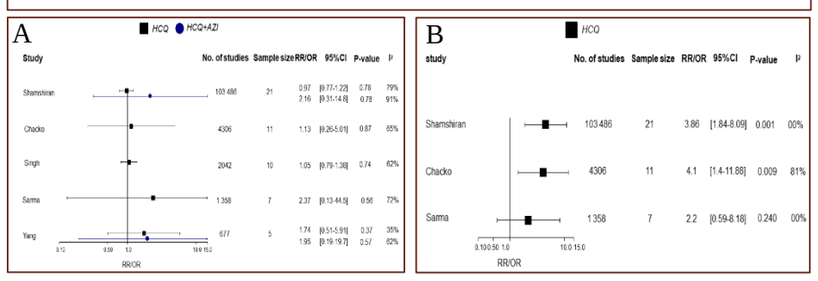


Figure 4. Results from meta-analyses included assessing A. virological cure and B. Adverse events.

Results of the updated meta-analysis of experimental studies

All-cause of mortality

There was no significant difference in risk of mortality between participants who received HCQ with or without Azithromycin and those on standard care (Fig 5).

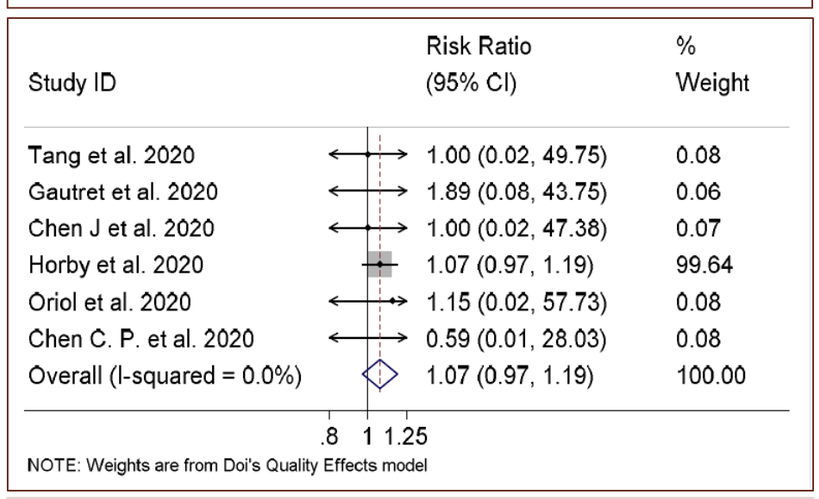


Figure 5. Results from our updated meta-analysis assessing all-cause mortality.

Secondary outcomes

No significant differences between the groups in the risks of ICU transfer/mechanical ventilation, virological cure, and disease exacerbation. There was a significantly higher risk of adverse events in participants who received HCQ compared to those on standard care (Fig 6).

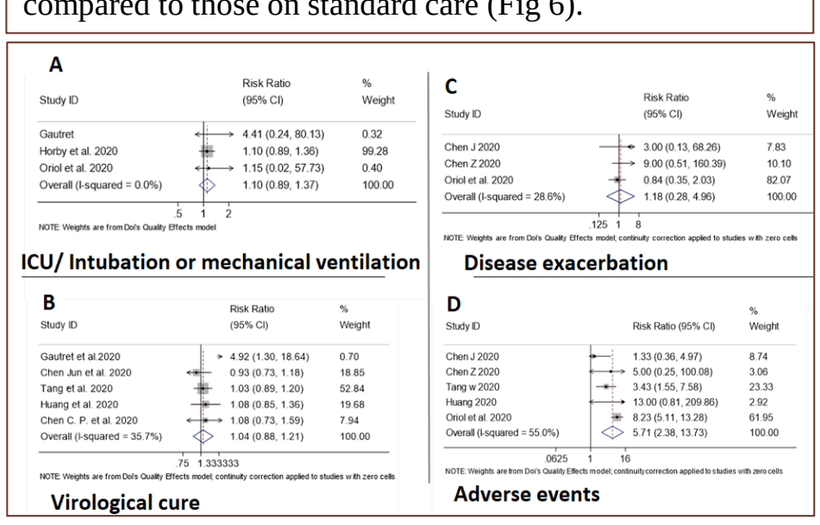


Figure 6. Updated meta-analysis of experimental studies on secondary outcomes.

Conclusion

- There is conclusive evidence that CQ and HCQ, with or without Azithromycin are not effective in treating COVID-19 or its exacerbation.

References

- Singh AK, et al. "Hydroxychloroquine in patients with COVID-19: A Systematic Review and meta-analysis.". Diabetes Metab Syndr.14(4):589-96.
- Chacko J, et al. Hydroxychloroquine in COVID-19: A systematic review and meta-analysis. medRxiv. 2020.
- Shamshirian A, et al. Hydroxychloroquine Versus COVID-19: A Periodic Systematic Review and Meta-Analysis. MedRxiv. 2020.