Genomic markers associated with respiratory syncytial virus (RSV) disease severity in children: A systematic review.

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BACKGROUND

- Respiratory syncytial virus (RSV) is the second most common cause of death in children under one year of age, and infects most children by the age of two years [1,2].
- The clinical manifestations of RSV vary from mild, self-limiting illness to life-threatening disease.
- The majority of children who develop severe RSV disease requiring hospitalisation have no apparent pre-existing risk factors.
- Genetic factors are known to affect susceptibility to severe infections in infancy and childhood [3].
- No established genomic markers that predict the severity of RSV bronchiolitis.
- This systematic review will inform the analysis of a large prospective cohort study.

OBJECTIVE

In this systematic review we aimed to identify genomic markers that are associated with severe RSV disease in children.

METHODS

- A systematic literature search was performed on the following databases: Ovid MEDLINE, Embase, Global health, Scopus and Web of Science, in November 2016, and additional papers were added from review of reference lists.
- We included human studies in children investigating the association between genomic markers and severity of RSV disease.
- We excluded studies in animal models or adults, epidemiological studies and studies without definitive RSV diagnosis.
- Broad search strategy to capture all possible genomic markers.
- Two authors independently assessed quality and risk of bias, with a third author available for resolving any disagreement.

RESULTS

- We identified 23 relevant papers (Figures 1 and 2) involving over 12,000 participants in total.
- We identified 14 single nucleotide polymorphisms (SNPs) and 6 further haplotypes associated with severe RSV disease (Figures 3-5).
- 15 SNPs did not have a statistically significant association with RSV severity.
- Conflicting results were reported for SNPs relating to RANTES, TLR4, IL-9 and TNF genes.
- Haplotypes of GC1 VDBP, TNF, IL-18, SP-B, TLR-10 and IL-8 were associated with RSV severity.

Figure 1. Study flowchart

Figure 2. Methodological quality graph

Figures 3-5. Relationship between RSV disease severity and single nucleotide polymorphisms (SNPs) associated with genes investigated

LIMITATIONS

- Large heterogeneity of studies.
- Small sample sizes in some studies.

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CONCLUSIONS

- Several SNPs and gene haplotypes were associated with severity of RSV disease.
- This may aid objective definitions of severe disease, understanding of mechanisms, and prediction of clinical outcomes.
- Future large scale studies should validate and replicate these studies.

INCLUDED STUDIES

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