Reviewer's report

Title: Reduced Dicer expression in the cord blood of infants admitted with severe respiratory syncytial virus disease

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Reviewer: natan noviski

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Overall this is an interesting and well written manuscript describing the relationship between expression of the Dicer ribonuclease at birth and the incidence of severe RSV infection in the first year of life.

Major compulsatory revisions:

1. The authors need to further clarify the issue of how severe RSV was defined. On one hand they mention in the methodology (page #7 second paragraph) that patients were categorized according to table 1 in which mechanically ventilated patients are included among the group with severe RSV infection. In the results section they mention that 20 patients who had severe RSV were included in their cohort study. On the other hand, in the discussion section (page 13 first paragraph) they mention that their cohort did not include patients requiring mechanical ventilation or CPAP. Please explain why they were excluded (if indeed they were excluded). Please, also clarify, in the results section, how many out of the 20 patients had each one of the characteristics that classified them as having severe disease. It is important to know if these were patients presenting with apnea, cardiovascular compromise, etc.

Minor essential revisions:

General comments:

The core issue of the paper is whether Dicer is decreased in neonates with severe RSV disease. If this is the case why aren't protein levels altered. The authors try to explain this in the discussion. Further explanation can be helpful for the reader to understand this paradox: Is the protein more sensitive to degradation and RNA not?

Specific comments:

1. Introduction: The rationale for the study is clearly laid out. However, a clear statement of the hypothesis stating the postulated relationship between Dicer and RSV infection in the last paragraph would be helpful.

The last paragraph on page 4: The last sentence should read “This mechanism is called RNA interference (RNAi), and is an important post-transcriptional regulator...”. Substitute “While” for “Whilst in the sentence later in this paragraph.

2. Methods:
2a. When “journals” are referenced in the second full paragraph on page 6 (Patient identification and clinical information) and in the first full paragraph on page 7, does this refer to medical records or journals completed by families participating in the birth cohort? Please clarify.

2b. Were the investigators reviewing the subjects’ medical records blinded to their Dicer status when determining the severity of RSV infection?

2c. Table 1: The majority of these data used in the algorithm are well defined. The definition of dyspnea is the exception to this as it seems quite subjective. Respiratory rate at admission would be a useful variable in the classification of disease severity. For future work, use of a validated symptom score may be useful.

3. Results: Figure 1: It is clearly stated in the text that the Dicer protein was present in the WiDr cells but not any of the other groups. Is it necessary to demonstrate it via Western blot?

3a. Did any of the 15 patients without sufficient RNA for analysis have documented RSV infection in the first year after birth?

3b. Table 3: pCO2, oxygen saturation, respiratory rate, and pulse are reported. Do these data represent the values upon admission? Mean values? Most severe values observed? Without this data this table is redundant.

3c. Figure 2: This requires further clarification. The values appeared higher for the severe patients. However, it is stated in the Statistical Analysis portion of the Methods that the ##Ct values were assigned a negative value.

4. Discussion: One of the primary issues with the paper is the inability to detect the Dicer protein in the subjects and controls. The authors provide a reasonable discussion, of this, however, and the mRNA measurement seems to be a reasonable proxy. As mentioned above, further explanation will be helpful.

4a. In the middle paragraph, page 15, the authors state that “we can hypothesize that Dicer downregulation would similarly result in greater RSV load, potentially promoting a negative pro-inflammatory viral effect”. The italicized clause should either be removed or further elaborated.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
We declare that we have no competing interests