

Peer Review File

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Reviewer A

Birth defects are defined as structural or functional abnormalities occurring during the development of the fetus in utero, which can be diagnosed before or at birth. In the manuscript “Independent factors associated with birth defects during the whole of pregnancy in Shenyang City, China”, authors analyzed the surveillance data of birth defects during the perinatal period and the whole of pregnancy, as well as the independent influencing factors.

Couple questions are required to be answered before it will be accepted.

(1) The independent factors associated with birth defects were the crucial topic in the paper. How about the progress of independent factors associated with birth defects? Please state in the introduction.

Reply (1): Thanks for your comments. We have modified our text as advised (see Page 3-4, line 96-102).

(2) It was better to add related reference (DOI: 10.3978/j.issn.2224-4336.2014.07.10) about the birth defects in the paper.

Reply (2): Thanks for your comments. We have added this reference and other references in the text.

(3) What is the means of “Ref.” in the table 4 and 5? Please state clearly in the table legends.

Reply (3): Thanks for your comments. It means that the data is invalid reference. We have added the meaning in the table legends.

(4) How about the roles of prenatal diagnosis in decreasing birth defects? Please supplement in the discussion.

Reply (4): Thanks for your comments. The text has been stated that most fetuses with severe and fatal birth defects, such as, congenital heart disease, Down’s syndrome, and digestive system malformations, can be diagnosed by prenatal screening and prenatal diagnosis. We have added more explanation in the text. (See Page 9, line 283-285).

(5) Compared to other regions, what were the clinical characteristics of birth defects in Shenyang City? Please state in the discussion.

Reply (5): We have explained the clinical characteristics of birth defects in Shenyang City in the first and second paragraph of the discussion.

(6) Whether the environment pollution was an independent influencing factor for birth defect? Please state in the discussion.

Reply (6): Thanks for your comments. We have modified our text as advised (see Page 10, line 328-330).

(7) It was showed that there was no significant change in the incidence of birth defects in this hospital from 2017 to 2020. With the technology development, it was common sense that the incidence of birth defects was decreased. Please supplement the explain about the no significant change in the incidence of birth defects in the discussion.

Reply (7): Thanks for your comments. We have modified our text as advised (see Page 10, line 315-321).

Reviewer B

1) First, the title is overstated since the data were collected from only on hospital in Shenyang, not all hospitals in Shenyang. Please also indicate the clinical research design in the title i.e., a retrospective cohort study.

Reply (1): Thanks for your comments. Our hospital is one of the three hospitals with the largest delivery volume in the local area, accounting for about 20% of the city's born population, so the data are representative to a certain extent. We have added the clinical research design in the title (see Page 1, line 3).

2) Second, the abstract needs some revisions. The background did not describe the knowledge gap on this research focus and what the clinical significance of this research focus is. The methods need to describe the inclusion criteria, assessment of potential risk factors, and diagnoses of birth defects, as well as main statistical methods for assessing the associated factors. The results need to briefly summarize the baseline clinical characteristics of the study sample. The conclusion should not repeat the findings again and please have comments for the clinical implications of the findings.

Reply (2): Thanks for your comments. We have modified our abstract as advised by editorial word count requirement (350 words is maximum)(see Page 2-3, line 50-78).

3) Third, the introduction of the main text needs to review what has been known on the incidence rate of birth defects and their associated factors and analyze the limitations of prior studies. Please also indicate the clinical significance of this research focus to support the clinical needs for this study. The identified factors associated with birth defects are not novel, therefore, the authors need to clearly indicate the novelty of this study.

Reply (3): Thanks for your comments. We have modified our text as advised (see Page 4, line 115-120).

4) Fourth, in the methodology of the main text, please accurately describe the clinical research design, the time-point of the data collection of potential risk factors, the calculation of the incidence rates of different subtypes of birth defects, and details of selecting significant factors from the multiple logistic regression.

Reply (4): Thanks for your comments. We have modified our text as advised (see Page 5, line 162 and Page 6, line 188-191).