DOES LIGHT DRINKING DURING PREGNANCY IMPROVE PREGNANCY OUTCOME? A CRITICAL COMMENTARY

Violette Gijsen, Netta Fulga, Facundo Garcia-Bournissen, Gideon Koren
The Motherisk Program, Hospital for Sick Children, Toronto

ABSTRACT

A recent study published from the University College London suggests that children of women who were light drinkers during pregnancy demonstrate better cognitive outcome at three years of age when compared to children of abstinent women based on data from the UK Millennium Cohort Study. Unfortunately, methodological pitfalls and limited external validity of the results presented make conclusions very tenuous. This paper was widely quoted by the media, sometimes concluding that drinking is beneficial. At the present state of knowledge, the poor quality of this study may cause more damage than benefit, as demonstrated by the media response.

A recent study published in the International Journal of Epidemiology by researchers from the University College London suggests that children of women who were light drinkers during pregnancy have better cognitive outcome at three years of age as compared to children of abstinent women based on data from the UK Millennium Cohort Study.[1]

The issue of cognitive effects of light drinking in pregnancy is an important one, given the number of women who actually consume limited amounts of alcohol often before realizing they have conceived. These results were rapidly quoted by the media, leading to a flurry of print and internet articles discussing the potential benefits of light alcohol exposure during pregnancy. The media presented the results of the study with varying degrees of accuracy, from suggesting that light drinking may lead to calmer babies[2] or even be good for babies,[3] to more balanced views suggesting that the study failed to find detrimental effects of light drinking on the children in the cohort.[4]

The suggestion that light drinking during pregnancy does not increase the risk of adverse consequences in the baby, and may even be associated to cognitive and behavioural benefits in boys, seems to have rapidly caught the public's attention. The issue of alcohol consumption during pregnancy is clearly very charged. While the relationship between heavy alcohol use during gestation and fetal alcohol spectrum disorder (FASD) has been proven beyond doubt,[5,6] the association between lower levels of exposure and detrimental cognitive effects on the offspring is far from being resolved. The actual risk that light drinking during pregnancy presents to the offspring is ill-defined at best and has been the subject of vivid discussions in the medical and lay literature.[2,3,4,7,8,9]

Unfortunately, the recent study by Kelly and colleagues, leading to the suggestion that light drinking during pregnancy is devoid of risks, is flawed and many of the conclusions disseminated in the press are not supported by its results. While some of the more radical affirmations found in the lay press relating to this paper are only remotely based on the results reported,[2,4] others[3] are quite close to what the authors of the study wrote, but nonetheless impossible to substantiate with the data presented.

In the study[1] Kelly and colleagues used data from the Millennium Cohort Project (MCP) to evaluate neuro-cognitive and behavioural outcome

of 12,500 children at approximately 3 years of age, and correlated them to maternal drinking history during pregnancy, as described by the mother. The study used data from two periods, the first "sweep" of the MCP, carried out between 2000 and 2002, and the second "sweep", carried out 3 years after the first. Data from the first sweep was used to evaluate maternal drinking during pregnancy, and involved women who had given birth approximately 9 months before the interview. Data from the second sweep was used to evaluate the cognitive and behavioural outcomes of those children at 3 years of age.

The cognitive evaluation of the children was carried out using the naming vocabulary subscale from the British Ability Scale (BAS) and the Bracken School Readiness Assessment (BSRA) scale. The behavioural evaluation was performed using the Strengths and Difficulties Questionnaire (SDQ), a scale based on parental reporting of children behaviour, as opposed to a formal evaluation by the interviewer. The authors used the data collected to define normal and abnormal values (i.e., above or below the 90 percentile for the data) as opposed to using values previously validated in other populations. These limits of "normality" may not be valid for other populations.

Several statistical models were used to correct for disbalances in covariates, with the more complex model correcting for multiple potential confounders such as maternal age, smoking, level of education, socio-economical status and other. One of the models suggested that boys born to mothers who were light drinkers had statistically higher cognitive scores than boys whose mothers were abstinent. The difference was observed initially in both the BAS and BSRA scales, but disappeared after controlling for other factors in the BAS scale (but not the BSRA). Interestingly, the authors do not mention in their discussion that boys of moderate drinkers also had statistically significant higher BAS scores, even after controlling for other factors.

No statistically significant effects were observed in girls in any of the cognitive or behavioural scales or in boys in any of the other drinking categories. This is the main point that was picked up by the papers, namely that light drinking did not have worse outcome (and maybe even the contrary), compared to abstinence; based on the absence of statistically significant differences among the two groups. A few warnings come to mind when evaluating the evidence presented. First, absence of evidence is not evidence of absence, meaning that a non-significant difference does not mean that there is no difference at all, but rather that it is possible that the study was not sufficiently powered to find it. It is also possible that, as discussed below, confounders such as subject misclassification (e.g., drinkers who denied drinking) could have biased the result towards "no difference".

It is important to note that not only the light drinkers did not do worse than the abstinence group, the moderate and heavy drinkers did not do worse either. In fact, if we were to accept the authors' conclusions as true, we would have to believe that alcohol does not have any relationship to the outcome in the children of this cohort, except maybe in improving some of the outcomes. This conclusion would go against a large body of evidence supporting a detrimental role of alcohol in pregnancy.[10,11,12]

The method for screening of maternal alcohol consumption during pregnancy was simply asking the mothers whether they drank and how much. Accordingly, four drinking categories were defined: never, light, moderate and heavy/binge. It has been well established that maternal self-reports of alcohol use are often unreliable due to fears of stigmatization, embarrassment, shame or guilt.[13,14,15] In addition to the fact that self-reports are unreliable, the danger of drinking during pregnancy has been repeatedly laid out in the press worldwide, including the UK.[7,8] It is unlikely that pregnant women would be unaware of the risks presented by drinking in pregnancy. Consequently, women in the study could have misrepresented their drinking habits, downplaying how much they actually drank in pregnancy, afraid that they would be judged if they told the truth or even that their children would be taken away.

In addition, the results suggest that a larger proportion of the mothers were drinking when the children were 3 years of age (at the time of the second interview). This further begs the question how many of these women were actually drinking during pregnancy, but declared to have been abstinent. There are tools for screening of alcohol misuse in women that have been found to be both

sensitive and specific. In "Fetal Alcohol Spectrum Disorder: Canadian guidelines for diagnosis"[16] it is recommended that all pregnant and post-partum women should be screened for alcohol use with validated screening tools (i.e., T-ACE, TWEAK) by trained health care providers. Along the same line, a study published in April 2008[17] investigated whether biomarkers of alcohol consumption would provide additional information to the use of a validated alcohol questionnaire in pregnant women. The women completed a questionnaire (AUDIT) and in addition, urine and hair samples were collected to detect direct ethanol metabolites. Urine samples were used for detection of ethyl glucoronide (EtG) and ethyl sulphate and hair samples were tested for EtG and Fatty Acid Ethyl Esters (FAEE). The results led to the conclusion that the combined use of the AUDIT questionnaire and samples for direct ethanol metabolites detect more potential alcohol consumers than any of these tests on its own. Another study published earlier this year[18] suggested that determination of FAEE and EtG in hair could serve as a promising way for retrospective detection of alcohol abuse during pregnancy. On the other hand, when there is no information on maternal drinking, it is still possible to test for alcohol metabolites in meconium, the first fecal excretion of newborns. Studies have shown high levels of FAEE in meconium of babies born to mothers who admitted drinking.[19,20] Meconium begins to form at about 14 weeks' gestation, thus, positive test results indicate maternal drinking during the second and third trimesters of pregnancy. Clearly, the method employed by Kelly et al for determination of alcohol use during pregnancy, relying on brief questioning of the women, was inadequate and could lead to serious bias in the results.

The women who were lost to follow up between the first and the second interviews did not seem representative of the rest of the sample, being younger, less educated and with lower household incomes than the mean of the population. While we do not know to which (drinking) groups they belonged to, and hence it is not possible to know how this attrition might have biased the results, it is conceivable that more severe cases would be overrepresented among the drop-outs, which could drag the scores of the higher exposure group towards those of the others.

The differences observed in the types of jobs and socio-economical status among the groups (e.g., the light and moderate drinkers had higher average income and education than the abstinent and high drinking groups) might have influenced many aspects of the relationship between the mothers and their children that could in turn affect the outcome of the study. It is very evident that the "mild drinkers" were of higher socio-economic status and earning, and probably higher IQ than the abstainers. All these would affect the main outcome of the study, and although the authors purport to "correct" for these differences in their statistical model, they could control only for what they had, and they had very little. This is one of the biggest fallacies of epidemiological studies: you control in multivariate analysis for what you have, and cannot claim that the groups are otherwise equal. The fact that the abstainers were of lower education level and lower socio-economic status than the mild drinkers says volumes about the inability to assign "direct effect" to alcohol, itself. Indeed, the authors of the study found that children in the lowest household incomes had lower cognitive abilities as compared to children from the highest household incomes. This was already established in many previous studies due to the influence of the socio-economic status of this group of women and the problems that come along with it. Most importantly, in the fully adjusted models used by the authors only two results turned out to be significant. This may be due to chance alone as a direct result of the large number of comparisons that have been performed.

Certain important confounding factors are missing from the authors' statistical models. One of the most important predictors of child IQ is maternal IQ. It has been documented repeatedly that the IQ of the mother influences the cognitive outcome of the children, and not controlling for maternal IQ may produce biased results (e.g. if mothers with higher education had higher IQs, their children would be expected to fare better in cognitive tests[21,22,23]). Another confounding factor that was not included is maternal marital status (i.e. married, alone, living with a partner). These all have the potential to influence the cognitive

and behavioural outcomes of the children (e.g., a single mother with no support may have less time to dedicate to her children as compared to a mother with a partner). Additionally, we are not informed when during pregnancy the women actually drank alcohol. Since timing may affect the outcome of the children, it might have also influenced the results of the study.

Finally, this study explored associations and clearly cannot prove or even suggest causation. These results can be hardly be extrapolated to other countries where more heterogeneous and multicultural populations with a range of different ethnicities live.

CONCLUSION

The issue of cognitive effects of light drinking in pregnancy is an important one, given the number of women who actually ingest limited amounts of alcohol in pregnancy. The paper by Kelly et al does not allow an answer to the question "is light drinking safe in pregnancy?" The methodological pitfalls observed and the limited external validity of the results presented make conclusions frivolous.

It is imperative that well planned studies are carried out to address this important question. This question is not ludicrous, given the high number of exposed pregnancies, and the consequences of a clear answer would go well beyond the scientific field, into public policy and public health. At the present state of knowledge, the low quality of this study may cause more harm than benefit, as demonstrated by the media response.

Corresponding Author: *facugb@hotmail.com*

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