J Neurol (2012) 259:2246–2248
DOI 10.1007/s00415-012-6553-z

LETTER TO THE EDITORS

Breastfeeding and multiple sclerosis relapses: a meta-analysis

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Received: 29 March 2012 / Revised: 2 May 2012 / Accepted: 8 May 2012 / Published online: 23 May 2012

Dear Sirs,

An increased relapse rate immediately post-partum in multiple sclerosis (MS) patients is well established [1]; however, no consensus has been reached regarding the impact of breastfeeding on post-partum relapse risk. Women with MS make a difficult choice between not restarting disease-modifying drugs and breastfeeding, or restarting therapy and not breastfeeding, or curtailing the duration of breastfeeding. In this study we aimed to meta-analyse all available data to give a more accurate estimate of the impact of breastfeeding on the risk of post-partum relapse.

A comprehensive search of the PubMed database was undertaken using the search terms "breastfeeding" and "multiple sclerosis". There was no time period restriction. Abstracts of the identified studies were hand-searched to select studies comparing post-partum relapse occurrence in a breastfeeding (BF) versus not breastfeeding group (not BF). Studies were excluded if they were not available in English, an interventional drug trial where drug effect was the primary aim, or if they did not compare relapse occurrence in breastfeeding versus not breastfeeding mothers. Where a study was considered suitable for inclusion but raw data were not available, authors were contacted. In total 12 studies were selected for inclusion [2–11] (details found in Online Resource 1), of which for two unpublished data were obtained from KH, yielding a total of 869 MS patients who breast-fed versus 689 MS patients who did not.

The inverse variance with the random effects model in Review Manager 5.1 was used to calculate the overall odds ratio (OR) of having at least one post-partum relapse in MS patients who breastfeed versus those who do not, 95 % confidence interval (CI) and test statistic for heterogeneity. The Egger p value was calculated to assess publication bias.

Women who did not breastfeed were almost twice as likely to have at least one post-partum relapse [OR 0.53 (95% CI 0.34–0.82), Fig. 1]; however, significant heterogeneity was present ($P = 0.002$; $I^2 = 63$ %). A funnel plot showed no evidence of bias (Egger p value 0.67), Fig. 2. Sensitivity analysis showed that inclusion of only the eight prospective studies [3, 5–9, 11] had an OR = 0.46 (0.30–0.70) with no significant heterogeneity ($P = 0.18$, $I^2 = 32\%$). Four studies [2, 6, 8, 9] reported the pre-pregnancy relapse rate; this was not significantly lower in women who breastfed as compared to women who did not [mean relapse rate (MRR) 0.61 vs. 0.82; $P = 0.57$]. Three studies [6, 8, 9] reported data on the relapse rate during

Electronic supplementary material The online version of this article (doi:10.1007/s00415-012-6553-z) contains supplementary material, which is available to authorized users.

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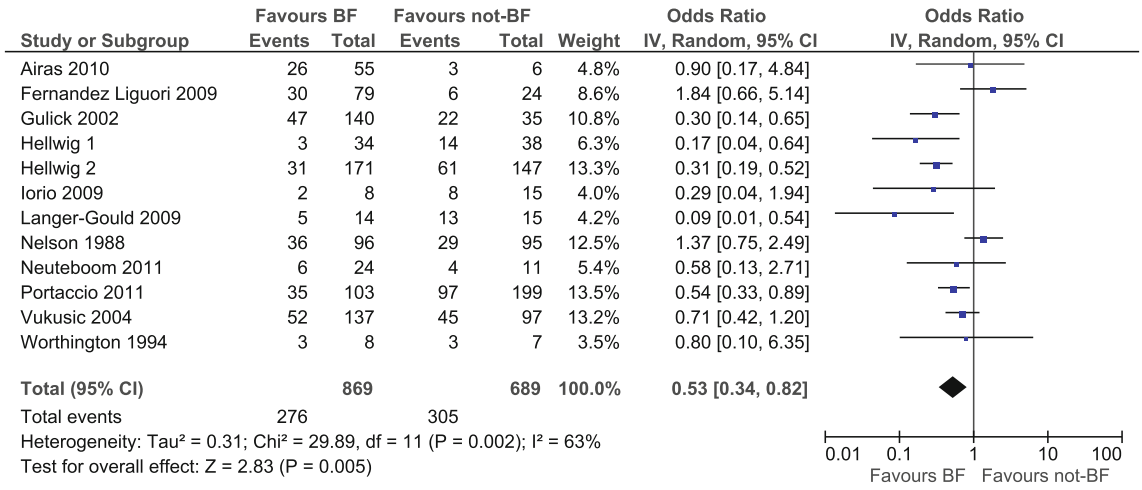

Fig. 1 Forrest plot of comparison: BF MS patients versus non-BF MS patients

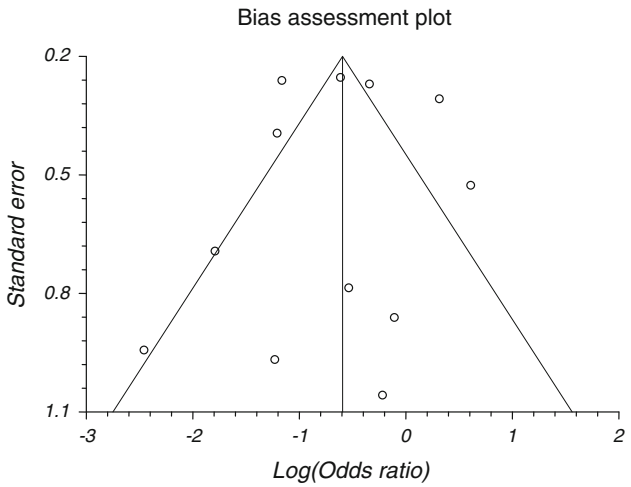

Fig. 2 Bias assessment funnel plot of included studies

pregnancy, which was not significantly lower in women who breastfed compared to women who did not (MRR 0.19 vs. 0.31; $P = 0.43$). One study reported EDSS at conception to be higher in women who did not breastfeed as compared to those who did (1.6 vs. 1.3; $P = 0.004$) [6]. Three studies [2, 3, 6] included data on the use of disease-modifying therapies (DMTs) before pregnancy; women who breastfed were significantly less likely to use DMTs than women who did not breastfeed ($P = 0.003$). Follow-up data were available a year post-partum for four studies [2, 3, 6, 8], 9 months for one study [4], 6 months for five studies [7, 8, 10, 11] and 3 months for two studies [11]. Sub-group analysis was done of the four studies that investigated 1-year post-partum, which generated an OR for at least one relapse of 0.35 (95 % CI 0.19–0.65) in those who breastfed, with non-significant heterogeneity ($P = 0.19$, $I^2 = 37$ %). Analysis was also done of the five studies that had data for 6 months post-partum [OR 0.59 (95 % CI 0.31–1.14)] with significant heterogeneity ($P = 0.04$, $I^2 = 56$ %). Subgroup analysis was also done of the five studies that defined BF as exclusive BF (for at least 2 months or of unspecified length), and comparing exclusive BF with non-exclusive BF and non-BF produced an OR 0.33 (95 % CI 0.19–0.55) for at least one relapse with insignificant heterogeneity ($P = 0.16$, $I^2 = 39$ %).

We found that women with MS who breastfeed are almost half as likely to experience a post-partum relapse compared to women who do not. While this suggests that breastfeeding has a protective effect on MS clinical activity, limitations include remaining heterogeneity (which we tried to dissipate as much as possible) and the fact that numerous studies relied upon accurate recall of breastfeeding history. Further, there is a strong possibility for confounding as shown by the finding that women who breastfed were significantly less likely to use DMTs before pregnancy, suggesting that the choice to breastfeed may be associated with more benign pre-pregnancy disease activity, and thus women with more severe MS may be less likely to breastfeed because of disability and/or in order to restart medication. Importantly, this study highlights the need for a large prospective study to assess the influence of breastfeeding on post-partum relapses in MS patients, with detailed measures of pre-, during and post-pregnancy disease characteristics and treatment recorded, in order to reach a robust conclusion as to whether breastfeeding truly influences disease outcome for MS patients, families and their caregivers.

Acknowledgments The authors would like to thank Prof. Christian Confavreux (Lyon, France), Prof. Sandra Vukusic (Lyon, France), Dr. Michael Hutchinson (Dublin, Ireland), Dr. Laura Airas (Turku, Finland) and Dr. Nora Fernández Liguori (Buenos Aires, Argentina) for kindly providing us with raw data from their studies. This work was funded by the Medical Research Council [grant no. G0801976]. No funding bodies had any role in the design and conduct of the study;

collection, management, analysis and interpretation of the data; and preparation, review or approval of the manuscript.

Conflicts of interest Ms. Pakpoor reports no disclosures. Dr. Disanto is funded by a research fellowship FISM-Fondazione Italiana Sclerosi Multipla-Cod.: 2010/B/5. Ms. Lacey reports no disclosures. Dr. Hellwig has received speaker honoraria and research support from Bayer Schering Pharma, Merck Serono, Biogen Idec, Pfizer Inc., Teva Pharmaceutical Industries Ltd.-Sanofi-Aventis. Prof. Giovannoni serves on scientific advisory boards for Merck Serono, Biogen Idec and Vertex Pharmaceuticals; served on the editorial board of Multiple Sclerosis; has received speaker honoraria from Bayer Schering Pharma, Merck Serono, Biogen Idec, Pfizer Inc., Teva Pharmaceutical Industries Ltd.–Sanofi-Aventis, Vertex Pharmaceuticals, Genzyme Corp., Ironwood and Novartis; has served as a consultant for Bayer Schering Pharma, Biogen Idec, GlaxoSmithKline, Merck Serono, Protein Discovery Laboratories, Teva Pharmaceutical Industries Ltd.–Sanofi-Aventis, UCB, Vertex Pharmaceuticals, GW Pharma, Novartis and FivePrime; serves on the speakers bureau for Merck Serono; and has received research support from Bayer Schering Pharma, Biogen Idec, Merck Serono, Novartis, UCB, Merz Pharmaceuticals, LLC, Teva Pharmaceutical Industries Ltd.–Sanofi-Aventis, GW Pharma and Ironwood. Dr. Ramagopalan receives research support from the Multiple Sclerosis Society of the UK.

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