O-075 The association between high birth weight and long-term outcomes-implications for Assisted Reproductive Technologies: a systematic review and meta-analysis

Å. Magnusson[1], H. Laivouri[2], A. Loft[3], N. Oldereid[4], A. Pinborg[3], L.B. Romundstad[5], M. Petzold[6], V. Söderström-Anttila[7], C. Bergh[1]

[1]Sahlgrenska University Hospital, Department of Gynecology and Reproductive Medicine, Göteborg, Sweden ;

[2]Tampere University Hospital and Faculty of Medicine and Health Technology, Department of Obstetrics and Gynecology, Tampere, Finland ;
[3]Copenhagen University Hospital, Fertility Clinic- Rigshospitalet, Copenhagen, Denmark ;
[4]Livio IVF-klinikken, Livio IVF-klinikken, Oslo, Norway ;
[5]Centre for Fertility and Health Norwegian Institute of Public Health- Oslo, Spiren Fertility Clinic, Trondheim, Norway ;
[6]University of Gothenburg, Swedish National Data Service & Health Metrics Unit, Gothenburg, Sweden ;
[7]University of Helsinki, University of Helsinki, Helsinki, Finland

Study question: Do high birth weight or large for gestational age (LGS) increase the risk of serious disease later in life?

Summary answer: High birth weight and/or LGA were associated with elevated risks for certain child malignancies, breast cancer, psychiatric disorders, childhood hypertension and diabetes type 1.

What is known already: Previous studies have shown that children born after frozen embryo transfer (FET) have an increased risk of being born LGA or having a high birth weight. In recent years the practice of FET in Assisted Reproductive Technology (ART) has increased rapidly. The perinatal risks of being born LGA or with a high birth weight are well studied, however less is known about the impact on long-term health and morbidity.

Study design, size, duration: Pubmed, Scopus and Web of Science were searched until December 2020. 11 748 abstracts were screened, 172 publications were selected for systematic review and 63 for meta-analyses. The methodological quality in terms of risk of bias was assessed by pairs of reviewers. Robin-I (www.methods.cochrane.org) was used for assessing risk of bias in original articles. For systematic reviews AMSTAR was used. For certainty of evidence the GRADE system was used.

Participants/materials, setting, methods: Exposures were LGA and high birth weight. Long-term morbidity outcomes were cancer, metabolic disease, cardiovascular disease and psychiatric disorders. Cancer was focused on breast cancer, child malignancies in the central nervous system (CNS), hematological malignancies and Wilm´s tumor. Metabolic diseases included diabetes type 1 and type 2. Cardiovascular diseases were focused on hypertension and other cardiovascular disorders and psychiatric disorders on schizophrenia/psychosis and cognitive disorders.

Main results and the role of chance: Pooled Adjusted Odds Ratios (AOR) for outcome variables were compared for birth weights >4000 or >4500 g versus <4000 g. For cancer, meta-analyses showed AOR of 1.24 (95% 1.11-1.39) for development of breast cancer, AOR of 1.15 (95% CI 1.05-1.27) for development of CNS tumors, AOR of 1.29 (95% CI 1.20-1.39) for childhood leukemia and AOR 1.68 (95% CI 1.38-2.06) for Wilm´s tumor.

For metabolic disease a meta-analysis showed AOR of 1.15 (95%CI 1.05-1.26) for the association between high birth weight and type 1 diabetes.

For psychiatric diseases an association was found between high birth weight and/or LGA and schizophrenia and depression.

For cardiovascular disease, an association was found between high birth weight and hypertension in childhood with an inverse association in adulthood. No difference in the risk of coronary heart disease in adults born with high birth weight compared to normal birth

Limitations, reasons for caution: The main limitation is that all data are based on observational studies with their inborn risk of selection bias. Our conclusions are however, mainly based on meta-analyses and/or studies with low risk of bias.

Wider implications of the findings: Even though high birth weight and LGA are associated with an increased risk of serious diseases, both in childhood and in adulthood, the size of these effects seems modest. However, the identified risk associations should be taken into account in stimulation strategies and when considering fresh or frozen embryo transfer.

Trial registration number: Not applicable