

# Heavy birthweight increases risk of developing rheumatoid arthritis

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People who have a birthweight over 10 pounds are twice as likely to develop rheumatoid arthritis when they are adults compared to individuals born with an average birthweight, according to a study published by researchers from Hospital for Special Surgery online in advance of print in the *Annals of the Rheumatic Diseases*. While the mechanism for this association is unclear, the study identifies a potentially modifiable risk factor and highlights a potential way to decrease the incidence of the disease.

"There may be a relationship between being born over 10 pounds and getting rheumatoid arthritis later in life," said Lisa Mandl, M.D., MPH, who led the study and is an attending rheumatologist at Hospital for Special Surgery (HSS) in New York City. "If there was some way that you could prevent someone from getting rheumatoid arthritis by making sure their birth weight wasn't over 10 pounds, this is a risk factor that could be modifiable. You can't change someone's age. You can't change someone's gender, but potentially you could change someone's birth weight. This is however only speculative at this point."

Previously, investigators have demonstrated that an increased risk of adult onset chronic disease can be a function of the fetal environment. Strong associations between low birth weight and an increased risk of type 2 diabetes mellitus, coronary heart disease and hypertension have been documented in a number of different populations. Published in 2003, a case-control study of roughly 400 individuals in Sweden identified an association between high birthweight and rheumatoid

arthritis.

To see if this association played out in a larger population, Dr. Mandl and colleagues turned to a study of 87,077 women in the Nurses' Health Study. In 1976, nurses were invited to participate in this study that involved a baseline survey and then a biennial questionnaire regarding health status, lifestyle, family medical history and health practices. The investigators excluded women who had cancer or any type of connective tissue disease at baseline or follow-up because these can cause joint swelling, symptoms that can be confused with rheumatoid arthritis. Also excluded were women who reported having rheumatoid arthritis or connective tissue disease during follow-up, but in whom the diagnosis could not be confirmed by review of their medical record. The study population included only women who answered a 1992 survey that collected information about birthweight. After these exclusions, 87,077 individuals were included in the study and 619 of them developed rheumatoid arthritis.

Through statistical analysis, the investigators discovered that a birthweight of greater than 4.54 kg doubled the risk that a person would develop rheumatoid arthritis as an adult compared with individuals who had an average birthweight.

"In utero, the fetus will react appropriately to different stressors. However, this may preprogram the fetus so that when it gets out into the world, this preprogramming is not helpful out in the 'real world'," said Dr. Mandl. In other words, the fetal environment may be preprogramming people's brains or endocrine systems to be maladapted in later life.

"There have now been two different groups, in different countries with different patients born at different times, that both suggest a similar relationship between birthweight and rheumatoid arthritis," said Dr.

Mandl. "I hope that other people will think about looking for this association in other populations."

Dr. Mandl says that patients with rheumatoid arthritis are known to have a dysregulated hypothalamic-pituitary-adrenal (HPA) axis, and this axis may be affected in utero. The HPA axis is the body's neuroendocrine system that involves the hypothalamus, pituitary and adrenal glands; this system is responsible for handling stress by regulating the production of cortisol, neurotransmitters and key hormones.

"If you look at this as a theoretic biologic underpinning for why this might be true, it might give basic scientists interesting ideas to think about regarding what causes rheumatoid arthritis, and provide support for a new hypothesis," Dr. Mandl said.

According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases, about 2.1 million people, or between 0.5 and 1 percent of the U.S. adult population, have rheumatoid arthritis, an autoimmune disease that causes chronic inflammation of the joints. The disease is more common in women and has no cure, but can be managed in a way that allows individuals to live productive lives.

Source: Hospital for Special Surgery

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