



Congress Review

Review of the 55th Annual Meeting of the European Association for the Study of Diabetes (EASD)

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Barcelona, Spain's mosaic masterpiece, created the breath-taking setting for the European Association for the Study of Diabetes (EASD) Congress 2019. Home to the remarkable La Sagrada Familia, the city welcomed >15,000 delegates from >130 countries, who attended the prestigious event. Amongst the colourful architecture in this cosmopolitan city, attendees to EASD were treated to a cornucopia of abstract presentations, stimulating symposia, and prize lectures. With such a wide range of content to consume, the EMJ team were spoilt for choice on what to cover for our review of this incomparable event in the field of diabetes.

EASD celebrated its 55th anniversary this year, and with the number of people affected by diabetes predicted to rise to 629 million by 2045, it is more critical than ever for diabetologists from all over the world to share knowledge and methods of best practice to improve the possibilities for diabetes diagnosis, treatment, and care. Some stand-out sessions at the congress focussed on a range of hot topics, including diabetic retinopathy, e-learning for diabetic complications, and the relationship between diabetes and the brain.

There were a huge 1,195 abstracts presented at EASD this year on a host of topics within the field of diabetes. We have hand-picked a selection of abstracts and present summaries of each within our congress review. These summaries are written by the researchers themselves, to offer a first-hand account of the work for our readers. Topics include trends in the incidence of prediabetes among immigrants in Canada and perception of living with diabetes gathered via a solutions-focussed therapy exercise through the medium of Twitter.

The air at EASD was buzzing with the influx of late-breaking research. Our review contains a write up of a selection of the most exciting press releases. One stand-out piece of research considered the link between babies being underweight and subsequently developing Type 2 diabetes mellitus as adults. Another press release covered the topic of



assisted reproductive technology increasing the risk of gestational diabetes. In the realm of diabetes treatment, another piece of late-breaking research considered the possibility of treating Type 2 diabetes mellitus with a combination drug approach: vildagliptin with metformin.

We interviewed four key opinion leaders, gaining insight into the field of diabetes from the experts. Dr Dorte Møller Jensen discussed the challenges of treating gestational diabetes and the key areas of focus in this area. Presenter of the session "My gut feeling about glucagon," Dr Filip Krag Knop, outlined the key takeaways for this session and discussed creating successful multi-disciplinary research partnerships. Prof Rayaz Malik took us through the main themes of his lecture "Diabetic neuropathy: A time to challenge the dogma," along with the purpose and importance of international study groups. In our final interview, Prof Steve Bain spoke to us about the elements of his job he finds most fulfilling and exciting updates in diabetic nephropathy research. As the field comes together and collaborates on better prevention and treatment for diabetes, it is inspiring to hear from these thought leaders on their specialist areas.

This year's 5-day meeting in Barcelona was another fantastic event from EASD, with a plethora of thought-provoking content on offer to attendees. Looking ahead to next year, we will be visiting Austria's capital city, Vienna, next September for the 56th EASD Annual Meeting, which is sure to be another unmissable event. But for now, we present our congress review of the brilliant EASD Annual Meeting from September 2019.

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Newly Diagnosed Type 2 Diabetes Mellitus May Be Optimally Treated Using a Combination Drug Approach

FOR PATIENTS newly diagnosed with Type 2 diabetes mellitus (T2DM), a combination therapy approach using vildagliptin and the first-line treatment metformin could result in better long-term blood sugar control and a reduced rate of treatment failure compared to treatment with the latter drug alone. This is according to findings presented at this year's EASD Congress in Barcelona, Spain, and reported in a press release dated 16th September 2019.

Vildagliptin belongs to a class of drug known as a DPP-4 inhibitor, and helps promote secretion of insulin by the pancreas, inhibition of glucagon production, and control of blood sugar levels.

To date, the recommended first-line treatment for T2DM has been metformin monotherapy, and combination therapy is only introduced in instances of treatment failure.

In the VERIFY study carried out by researchers from the University of Oxford, Oxford, UK, 2,001 patients from 254 centres in 34 countries were split into 2 groups: 1 in which 998 patients were randomised to receive early combination therapy of the 2 drugs, and the other in which 1,003 received metformin alone, both across a 5-year treatment period. The patients' level of HbA1c, a direct measure of blood sugar control, was assessed at multiple time-points across the treatment period.

In the initial period of the study, treatment failure (defined as HbA1c of at least 53 mmol/mol [7.0%]) occurred in 43.6% of patients in the combination treatment group, compared to 62.1% in the monotherapy group. Additionally, the chances of losing blood sugar control (i.e., HbA1c going above 53 mmol/mol [7.0%], twice) were approximately halved in the combination treatment group over the 5-year duration of the study. This sustained 'durability' was deemed to be the result of complementary mechanisms of action shared between both drugs.

Marcia Kayath, Global Head Medical Affairs and Chief Medical Officer, Novartis Pharmaceuticals summarised: "These promising results from the VERIFY study have the potential to improve patient outcomes and the way in which we treat T2DM in the future".

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An Approximately 6-fold Increase in Type 2 Diabetes Mellitus Linked to Obesity

CONSIDERING that the International Diabetes Federation (IDF) expects the number of people living with diabetes to rise above 600 million by the year 2045, there remains a strong need for improving the understanding of the genetic and environmental underpinnings of the disease. Reported in a EASD press release dated 16th September 2019, a group of researchers from the Novo Nordisk Foundation Center for Basic Metabolic Research in Copenhagen, Denmark, have revealed findings that associated obesity with a near 6-fold increase in risk for developing Type 2 diabetes mellitus (T2DM), and that an unfavourable lifestyle and high genetic risk were also implicated to a lesser, but still significant, degree.

In the analysis, 9,556 men and women from the Danish prospective Diet, Cancer and Health cohort were applied to a statistical model. T2DM developed, over an average of 14.7 years follow-up, in approximately half of the individuals (49.5%). An 'unfavourable' lifestyle was defined

as zero or one of four traits (moderate alcohol consumption, healthy diet, regular physical activity, non-smoker). Genetic risk was stratified into low, intermediate, and high based on a genetic risk score considering 193 genetic variants strongly associated with the disease.

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Obesity (defined as BMI ≥ 30 kg/m²) and an unfavourable lifestyle were found to be associated with an enhanced risk of T2DM across the cohort, where obesity in particular equated to a 5.8-fold risk increase.

The independent effects of genetic risk and lifestyle favourability were not as impactful; high genetic risk conferred a 2-fold increase, whereas a 20% increase in likelihood of diabetes development was associated an unfavourable lifestyle. "The effect of obesity T2DM risk is dominant over other risk factors, highlighting the importance of weight management in T2DM prevention," the authors concluded.



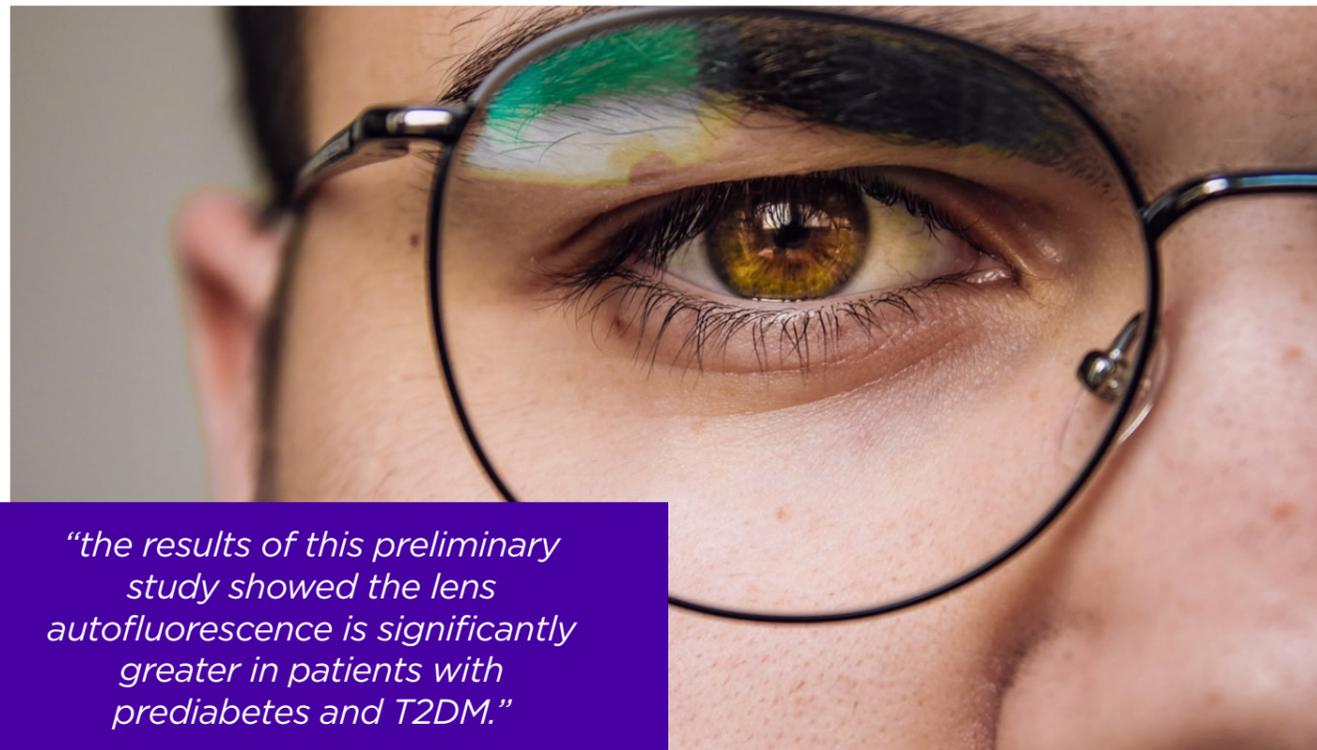
Noninvasive Analysis of the Eye Could Pre-empt Diabetes Risk

EARLY detection of Type 2 diabetes mellitus (T2DM) could help to prevent complications associated with the disease, including retinopathy and neuropathy. A press release dated 16th September 2019 from this year's EASD Congress in Barcelona, Spain, presented a study by Dr Mitra Tavakoli, University of Exeter Medical School, Exeter, UK, which showed that measuring the level of autofluorescence in the lens of the eye can be a useful tool in diagnosing patients with T2DM and impaired glucose tolerance, or prediabetes.

Prediabetes is a condition that can progress to T2DM. There can be a significant delay of up to 10 years between the onset of diabetes and diagnosis of the disease, during which time symptoms become increasingly worse. By predicting not only T2DM, but also prediabetes, complications arising from T2DM can be pre-emptively minimised. Increased levels of advanced glycation end-products (AGE) in those with T2DM are associated with worsening complications of the disease; therefore, by measuring the presence of AGE in the lens of the eye, the researchers were able to predict those at risk of developing T2DM.

The study recruited 20 participants with prediabetes, 20 with T2DM, and 20 control subjects, each of whom completed medical and neurological assessments. A beam of blue light was initially focussed onto the lens by a newly developed biomicroscope. The reflected green light allowed for the level of autofluorescence to be measured, giving a value for the AGE level in the eye. Dr Tavakoli said, "the results of this preliminary study showed the lens autofluorescence is significantly greater in patients with prediabetes and T2DM. The levels of AGE were correlated with the levels of blood sugar."

The substantial increase in AGE shown in participants with either T2DM or prediabetes compared to the control indicates that noninvasive specialist analysis of the lens of the eye could prevent complications occurring in those with undiagnosed diabetes by early detection. Dr Tavakoli concludes: "lens autofluorescence could be a robust marker of long-term diabetes control predicting future complication risks..."



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Reduced Risk of Type 2 Diabetes Mellitus by Delayed Onset of Menopause

EXPERIENCING puberty and menopause later in life is associated with reduced risk of Type 2 diabetes mellitus (T2DM); contrastingly, taking the contraceptive pill and increased menstrual cycle length is associated with a higher risk of developing the disease. This research was presented at this year's EASD congress in Barcelona, Spain, on 17th September 2019. The aim of the study was to explore the relationship between hormonal factors and T2DM risk in females.

The study, conducted by Dr Sopio Tatulashvili, Avicenne Hospital, Bobigny, France, and colleagues, incorporated 83,799 women from the French E3N prospective cohort study between the years 1992 and 2014. Estimation of risk and statistical significance between hormonal factors and T2DM risk was determined using computer models adjusted for risk factors including BMI, smoking, age, and family history of T2DM, amongst others.

The researchers established that participants who reached puberty aged over 14 years old versus under 12 years had a reduced T2DM risk of 12%. Those who were 52 years or over when they reached menopause had a 30% reduced T2DM risk compared to those who were aged 47 years or under. A 10% reduced risk of developing T2DM was observed in women who had breastfed compared to those who had never breastfed. The study also reported a reduced risk of developing T2DM in those who experienced a greater number of menstrual cycles throughout their lifetime. Experiencing over 470 cycles generated a reduced risk of 25% versus under 390 cycles. Longer time between puberty and menopause, over 38 years versus under 31 years, was also associated with a decreased risk of developing T2DM by 34%.

Risk of T2DM was increased by 33% in women who had taken contraceptive pills at least once in their lifetime, compared to those who had never used

them; additionally, participants who had greater menstrual cycle length, lasting over 32 days versus 24 days and under, was associated with a 23% increased risk. The authors said: "It seems that longer exposure to sex hormones but later in life could reduce the risk of later developing T2DM, independent of well-established risk factors..."

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Positive Effects from Alcohol Consumption in People with Type 2 Diabetes Mellitus



ALCOHOL consumption in people with Type 2 diabetes mellitus (T2DM) may exert positive results according to a press release on 17th September at the EASD congress in Barcelona, Spain. A meta-analysis investigating the effects of alcohol consumption on glucose and lipid metabolism has shown that recommendations to moderate alcohol consumption for people with T2DM may need to be reviewed.

The study by Yuling Chen, Southeast University, and Dr Li Ling, Director of the Department of Endocrinology, Zhongda Hospital and School of Medicine, Southeast University, Nanjing, China, analysed randomised controlled trials (RCT) that assessed the association between alcohol consumption and glucose and fat metabolism in adults with T2DM. Clinical trials were extracted from PubMed, Embase, and Cochrane up until March 2019. The sourced RCT data was then analysed using computer modelling.

In total, 10 relevant RCT were found, which included 575 participants, and were included in the review. Meta-analysis revealed decreased triglyceride and insulin levels associated to

alcohol consumption; however, no statistically significant effects on glucose levels, glycated haemoglobin, or total cholesterol were found. Further subgroup analysis delineated decreased levels of triglycerides and insulin in accordance with light to moderate amounts of alcohol (≤ 20 g alcohol per day), which translates to approximately 330 mL of beer (5% alcohol), 200 mL glass of wine (12% alcohol), or a 50 mL serving of 40% alcohol spirit (e.g., gin or vodka [40% alcohol]).

“Larger studies are needed to further evaluate the effects of alcohol consumption on blood sugar management, especially in patients with T2DM.”

Regardless of the effects on metabolism that the analysis has revealed, various diabetes organisations, including Diabetes UK, advise that people with T1DM and T2DM are cautious with their alcohol consumption, because drinking increases the risk of a hypoglycaemic episode and can additionally cause weight gain and other health issues.

The authors noted that “findings of this meta-analysis show a positive effect of alcohol on glucose and fat metabolism in people with T2DM. Larger studies are needed to further evaluate the effects of alcohol consumption on blood sugar management, especially in patients with T2DM.”

Certain Jobs Linked to Higher Risk of Type 2 Diabetes Mellitus



PROFESSION and risk of developing Type 2 diabetes mellitus (T2DM) have been linked according to a new study which was revealed in a press release at this year’s EASD on 18th September 2019. The study has shown that professional drivers, manufacturing workers, and cleaners have a three-fold increased risk of T2DM compared to other occupations such as teachers and physiotherapists.

Dr Sofia Carlsson, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, considered the possible association between the 30 most common occupations and T2DM. Dr Carlsson and her team speculated that the differences are linked to the prevalence of lifestyle risk factors; therefore, workplace interventions to reduce weight and increase physical activity would be beneficial to improve the health of the workforce.

All Swedish citizens born between 1937 and 1979 were identified using the Swedish Total Population Register and of these 4,550,892 people were gainfully employed between 2001 and 2013. The Longitudinal Integrated Database for Health Insurance and Labour Market Studies (LISA) was used to acquire information on occupation and education; employment was categorised under the Swedish Standard Classification of Occupations. In addition, a person had to have worked in that occupation for 2 consecutive years to be categorised into a specific occupation. From 2006 until 31st December 2015, follow ups for incidence of diabetes at age 35 or over was performed using the National Patient Drug Register.

The results highlighted major differences amongst the occupational groups. In 2013 the prevalence of diabetes was 4.2% (5.2% men; 3.2% women) in the Swedish working population. In men the prevalence ranged from 2.5% in computer scientists to 7.8% in manufacturing labourers and 8.8% in motor vehicle drivers. In comparison, the prevalence in women ranged from

1.2% in specialist managers to 5.5% in kitchen assistants and 6.4% in manufacturing workers. A separate analysis for those over 55 years of age showed that the prevalence in men was 13.1%, 14.2%, and 14.9% for office clerks, motor vehicle drivers, and manufacturing workers, respectively. In women over 55 years the prevalence was 8.3%, 8.7%, and 10.7% for cleaners, kitchen assistants, and manufacturing workers, respectively.

Further analysis uncovered a 49% higher risk of developing diabetes in male manufacturing, and a 80% higher risk in female manufacturing workers compared with the total Swedish working population. Male college and university teachers showed a 46% reduced incidence and female physiotherapists and dental hygienists a 45% reduced incidence. The study also highlighted a strong positive correlation between incidence of T2DM and BMI in both genders.

According to the authors “the association between occupation and T2DM coincided with vast differences in prevalence of lifestyle factors - individuals in high risk occupations were more likely to be overweight, smoke, and have lower physical fitness than those in low risk occupations, and this most likely contributes to a high prevalence and incidence of T2DM.” In conclusion the authors noted that intervention studies have proven that it is possible to reduce diabetes incidence in high-risk groups through lifestyle modification; therefore, if a job title can be used as a risk indicator for T2DM they can be targeted to implement diabetes prevention interventions.

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“Remarkable” Findings on Diabetes Prediction Possibilities



“It’s remarkable that we can see signs of adult diabetes in the blood from such a young age”

PREDICTION of a person’s likelihood of developing Type 2 diabetes mellitus (T2DM) later in life could help clinicians to prevent development of the disease at a much earlier stage, a EASD press release dated 18th September 2019 reports. The findings of a study co-led by Dr Joshua Bell, MRC Integrative Epidemiology Unit, University of Bristol, Bristol, UK, suggest that predictions could be made in children as young as 8 years of age using genetic testing and metabolomics to identify trends that could indicate a predisposition to T2DM.

The study enrolled 4,000 participants from the Children of the 90s study in Bristol, which began in the early 1990s. The participants were all healthy and generally free of chronic diseases such as T2DM. They were assessed using a genetic risk score for adult T2DM and each was assessed four times: aged 8, aged 16, aged 18, and aged 25 years, each time looking at >200 metabolic traits.

The participants who were most susceptible to T2DM were found to have a reduced levels of

high-density lipoprotein (HDL) cholesterol at age 8 before other types of cholesterol including low-density lipoprotein (LDL) were raised. Their inflammatory glycoprotein acetyls and amino acids were raised by 16 and 18 years old. These differences became more pronounced over time. Dr Bell explained the significance of these results, saying “It’s remarkable that we can see signs of adult diabetes in the blood from such a young age; this is about 50 years before it’s commonly diagnosed.”

Despite this being a big step forward in understanding about who may be more likely to develop this chronic disease later in life, this is just a small step in the overall goal for diabetes researchers. Dr Bell added: “If we want to prevent diabetes, we need to know how it starts. Genetics can help with that, but our aim here is to learn how diabetes develops, not to predict who will and will not develop it. Other methods may help with prediction but won’t necessarily tell us where to intervene.”

New Findings on Gluten Intake and Type 1 Diabetes Mellitus Risk

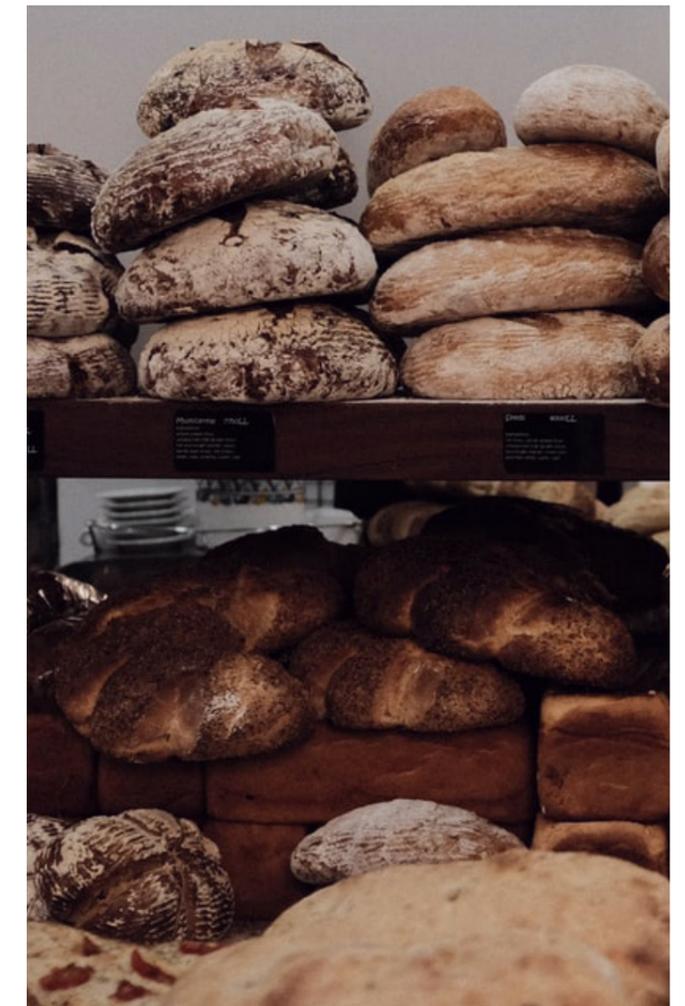
GLUTEN intake in a child at 18 months of age is a greater indicator of later development of Type 1 diabetes mellitus (T1DM) than maternal gluten intake during pregnancy, according to the findings of a study reported in a EASD press release dated 19th September 2019. The Norwegian Mother and Child Cohort Study found no association between maternal gluten intake during pregnancy and development of T1DM in her child.

In the first study to examine both maternal gluten intake during pregnancy and child’s gluten intake at age 18 months, 86,306 children born between 1999 and 2009 were enrolled and followed up until April 2018. The primary endpoint was clinical T1DM, confirmed using a nationwide childhood diabetes registry. The data was collected using a semi-quantitative questionnaire about food frequency at Week 22 of pregnancy and at child’s age 18 months, completed by the guardian. Statistical modelling was used to calculate increased risk for each subgroup.

A total of 346 children (0.4%) developed T1DM (incidence rate: 32.6 per 100,000 person-years) during a mean follow-up period of 12.3 years. The average gluten intake was 13.6 g/day for mothers during pregnancy, and 8.8 g/day for the child at 18 months of age. Gluten intake in children at 18 months of age was associated with an increased risk of later developing T1DM; the risk increased by 46% for each 10 g per day increase in gluten intake. Maternal gluten intake in mid-pregnancy, however, was not associated with T1DM development in the child.

Commenting on the findings, the authors explained: “There is some evidence that gluten intake may influence the gut microbiota and induce inflammation in so-called ‘leaky gut’ (increased absorption of dietary antigens

and/or gut infections). These are plausible mechanisms, but the exact mechanism explaining our findings is not known. If anything, we believe that gluten works in combination with another environmental factors such as virus infections in predisposed children.” They caution that the results of the study are not conclusive enough to warrant the avoidance or reduction of gluten in children’s diets; confirmation of the results from future studies is necessary before recommendations can be made: “Our observations may motivate future interventional studies with reduced gluten intake to establish whether there is a true causal association between amount of gluten intake in the child’s early diet and T1DM in susceptible individuals.”



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Assisted Reproductive Technology Linked to Gestational Diabetes

GESTATIONAL diabetes is more common in women who undergo assisted reproductive technology (ART) treatment, than in women who conceive naturally, as found in a study presented in a press release at EASD on 19th September 2019. The meta-analysis, which studied an estimated 2 million women, found that fertility treatments, such as *in vitro* fertilisation (IVF) and intracytoplasmic sperm injection (ICSI), increased the risk of diabetes.

The research team completed a meta-analysis and systematic review of 38 studies (with 17 matched controls and 21 unmatched controls) which compared the risk of gestational diabetes in women who underwent spontaneous conception, with those who had singleton pregnancies from IVF and ICSI. Data from 2 million women, and 163,302 gestational diabetes cases, was analysed. Women in the ART group were found to be 53% more likely to have gestational diabetes than the spontaneous conception group.

Researcher Dr Panagiotis Anagnostis, Aristotle University of Thessaloniki, Thessaloniki, Greece, discussed the study: “This rigorous assessment of the best available evidence to date shows that singleton pregnancies achieved by IVF are linked with an increased risk of developing gestational diabetes compared with pregnancies conceived naturally.”

In a further analysis of 17 studies, including 21,606 women, which matched participants for age, weight, height, smoking status, and ethnicity, it was found that ART singleton pregnancies resulted in a 42% higher chance of developing gestational diabetes, than in women who conceived naturally.

While this link was observed in the analyses, further study would be needed to confirm the findings as no solid conclusions can be drawn due to the observational method of the research. The researchers recognised the lack of adjustment for important confounders in the study. “The exact mechanism is unclear, and whether this risk is due to the medical intervention or the underlying infertility status of the couples undergoing assisted reproduction, is not yet fully understood and requires further research,” concluded Dr Anagnostis.



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Babies Born Underweight are more Likely to Develop Type 2 Diabetes Mellitus Earlier



UNDERWEIGHT babies are known to be at an increased risk of developing Type 2 diabetes mellitus (T2DM) as adults. Furthering this concerning association, new research from a study that investigated the onset age of T2DM and the physical characteristics of the disease, presented in an EASD press release dated the 19th September, found that underweight babies are younger by >1 year at T2DM diagnosis.

Involving >48,000 individuals who were enrolled in the Walker Birth Cohort (born in Dundee, UK, between 1952 and 1966) and were on the Scotland's national diabetes registry, the observational study investigated the impact of low birthweight on the phenotype of T2DM. Factors included were age at diagnosis, BMI, kidney function (creatinine levels), liver function (serum alanine aminotransferase), high-density lipoproteins (HDL)-cholesterol, triglycerides, and systolic blood pressure. Those born with a weight <2.9 kg were considered to be underweight.

In addition to a younger age of onset of T2DM at 50.0 years versus 51.3 years in babies born >3.6 kg, babies born <2.9 kg had a lower BMI at diagnosis (34 [obese] versus 36 [severely obese]) and had higher HDL-cholesterol at diagnosis (1.13 mmol/L versus 1.09 mmol/L). Furthermore, it was

found that this age of onset of T2DM in those with a low birthweight occurred irrespective of their adulthood BMI and HDL-cholesterol.

Providing a possible explanation for these results, the researchers concluded that reduced insulin secretion, both in the womb and later in life, could be the link between a low birthweight and age of T2DM onset. “This link between low birthweight and age of onset of diabetes may reflect common genetic factors that both mediate birthweight and diabetes risk, or intrauterine factors such as nutrition or maternal smoking, or the combination of the two,” commented the study conductor Mr Christian Paulina, a medical student from the University of Dundee, Dundee, UK.

“This link between low birthweight and age of onset of diabetes may reflect common genetic factors that both mediate birthweight and diabetes risk”