For private circulation only

Volume 89 | Issue 123 | Aug-Sep. 2020

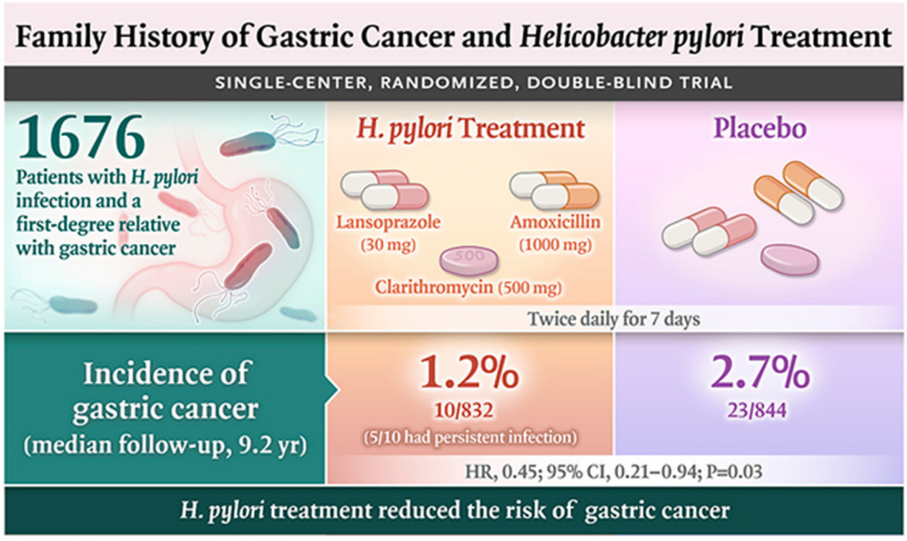
Fasting Diet
- Page 7

Preterm delivery and long term mortality in women: national cohort and co-sibling study.
- Page 11

Health Digest

ORIGINAL ARTICLE

1 Family History of Gastric Cancer and *Helicobacter pylori* Treatment



BACKGROUND

Helicobacter pylori infection and a family history of gastric cancer are the main risk factors for gastric cancer.

METHODS

In this single-center, double-blind, placebo-controlled trial, 3100 first-degree relatives of patients with gastric cancer were screened . Randomly assignation of 1838 participants with H. pylori infection to receive either eradication therapy (lansoprazole [30 mg], amoxicillin [1000 mg], and clarithromycin [500 mg], each taken twice daily for 7 days) or placebo. The primary outcome was development of gastric cancer. A prespecified secondary outcome was development of gastric cancer according to H. pylori eradication status, assessed during the follow-up period.

Dear Doctor,

We are proud to publish the next issue of the "Health Digest" written exclusively for medical professionals for their education and well-being.

Enjoy reading…

Editor:
Dr. Juma Venkatesh

Email:
md@glocarelabscro.com

CONCLUSIONS

Among persons with *H. pylori* infection who had a family history of gastric cancer in first-degree relatives, *H. pylori* eradication treatment reduced the risk of gastric cancer.

In this trial, the risk of gastric cancer was 55% lower among participants assigned to the group that received treatment for *H. pylori* infection than among those assigned to the placebo group and 73% lower among participants

in whom *H. pylori* eradication was confirmed than among those who had persistent infection.

These results are similar to those of our previous trial in patients with early gastric cancer (the risk of gastric cancer was 50% lower in the treatment group and 68% lower among participants in whom H. pylori was eradicated).

VISUAL ABSTRACT Family History of Gastric Cancer and *Helicobacter pylori* Treatment

Helicobacter pylori infection is a common bacterial infection of the human stomach that affects more than half the world population.

Two nested case–control studies conducted in the United States showed an association between *H. pylori* infection and gastric cancer.

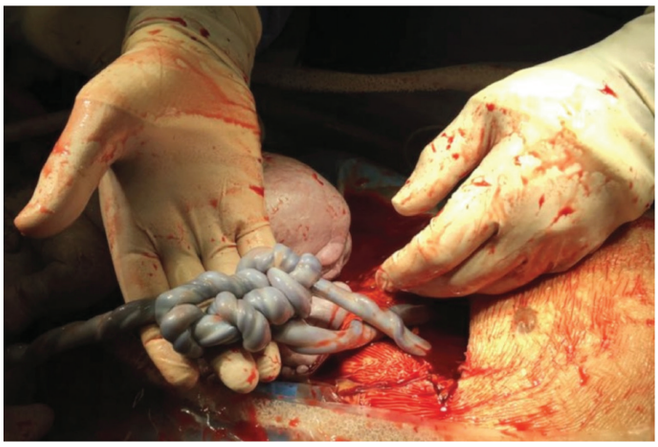
Recent randomized trial involving patients with early gastric cancer (a population that usually has severe atrophic changes in the gastric mucosa) showed that treatment of *H. pylori* infection reduced the risk of metachronous gastric cancer by 50%.Treatment of *H. pylori* infection in the general population to prevent gastric cancer is supported by moderate-quality evidence from a meta-analysis of six randomized trials that showed a relative risk of cancer .

A family history of gastric cancer in a first-degree relative is associated with double to triple the risk of gastric cancer.Patients with gastric cancer and their relatives share risk factors, including exposure to *H. pylori* in the environment and genetic features that may affect immune responses to *H. pylori* infection. Family members of patients with gastric cancer have higher rates of *H. pylori* infection than persons in the general population, and the precancerous histologic changes in the gastric mucosa are more severe in these persons.However, whether treatment of *H. pylori* infection can reduce the risk of gastric cancer is still unclear because of a lack of evidence from trials in primary prevention. Despite the uncertainty, regional and global consensus reports recommend treatment of *H. pylori* infection in the relatives of patients with gastric cancer

IMAGE CHALLENGE

Umbilical Cord Knot

A 36-year-old woman (gravida 2, para 1) with a monochorionic, monoamniotic twin pregnancy was admitted to the hospital at 32 weeks of gestation for a planned cesarean section. The antenatal course had been unremarkable. Routine cardiotocography before the procedure showed severe variable decelerations of the fetal heart rate in one of the twins; the tracing in the other twin was normal. A cesarean section was subsequently performed, and twin girls were delivered. The Apgar scores for both twins were 7 at 1 minute and 8 at 5 minutes. Complex knots in the umbilical cords were seen after delivery. Results of blood gas analysis of cord blood were normal. True knots in the umbilical cord are associated with intrapartum complications and fetal distress. Complex knotting to the extent seen in this case in the umbilical cords of monochorionic twins is uncommon. The twins were admitted to the neonatal intensive care unit, and both were discharged from the hospital after 40 days.



2 The Effect of Irbesartan on the Development of Diabetic Nephropathy in Patients with Type 2 Diabetes

BACKGROUND

Microalbuminuria and hypertension are risk factors for diabetic nephropathy. Blockade of the renin–angiotensin system slows the progression to diabetic nephropathy in patients with type 1 diabetes, but similar data are lacking for hypertensive patients with type 2 diabetes. We evaluated the renoprotective effect of the angiotensin-II–receptor antagonist irbesartan in hypertensive patients with type 2 diabetes and microalbuminuria.

CONCLUSIONS

Irbesartan is renoprotective independently of its blood-pressure–lowering effect in patients with type 2 diabetes and microalbuminuria.

Diabetic nephropathy develops in approximately 40 percent of all patients with type 2 diabetes and has become the leading cause of end-stage renal disease Therefore, the early identification and subsequent renoprotective treatment of all patients at risk are of utmost importance. The screening of urine for albumin has revealed that patients with type 2 diabetes and so-called microalbuminuria — i.e., a urinary albumin excretion rate of 20 to 200 µg per minute — have a risk of diabetic nephropathy that is 10 to 20 times that of patients with normoalbuminuria. Diabetic nephropathy develops in 5 to 10 percent of patients with type 2 diabetes and microalbuminuria each year. Blockade of the renin–angiotensin system slows the progression to diabetic nephropathy in patients with type 1 diabetes and microalbuminuria, but similar data are not available for hypertensive patients with type 2 diabetes.

We therefore undertook a multinational, double-blind, randomized study to evaluate the effectiveness of the angiotensin-II–receptor antagonist irbesartan in delaying or preventing the development of diabetic nephropathy in hypertensive patients with type 2 diabetes and persistent microalbuminuria. The optimal renoprotective dose of irbesartan was also evaluated.

DISCUSSION

Our study demonstrates that treatment with irbesartan significantly reduces the rate of progression to clinical albuminuria, the hallmark of overt diabetic nephropathy in patients with type 2 diabetes. Furthermore, the restoration of normoalbuminuria was significantly more common in the group receiving irbesartan at a dose of 300 mg daily. These benefits appear to be independent of the systemic blood pressure, since the average trough blood pressure during the study was only minimally lower in the irbesartan groups than in the placebo group, with no difference in diastolic blood pressure and a difference of 1 to 3 mm Hg in systolic blood pressure. Furthermore, a statistical analysis that adjusted for these small differences confirmed the renoprotective effect of irbesartan. Finally, kidney function remained well preserved in all groups.

IN CONCLUSION

Irbesartan is renoprotective independently of its blood-pressure–lowering effect in hypertensive patients with type 2 diabetes and microalbuminuria.

Case Review

3

Disseminated subcutaneous nodules and destructive polyarthritis

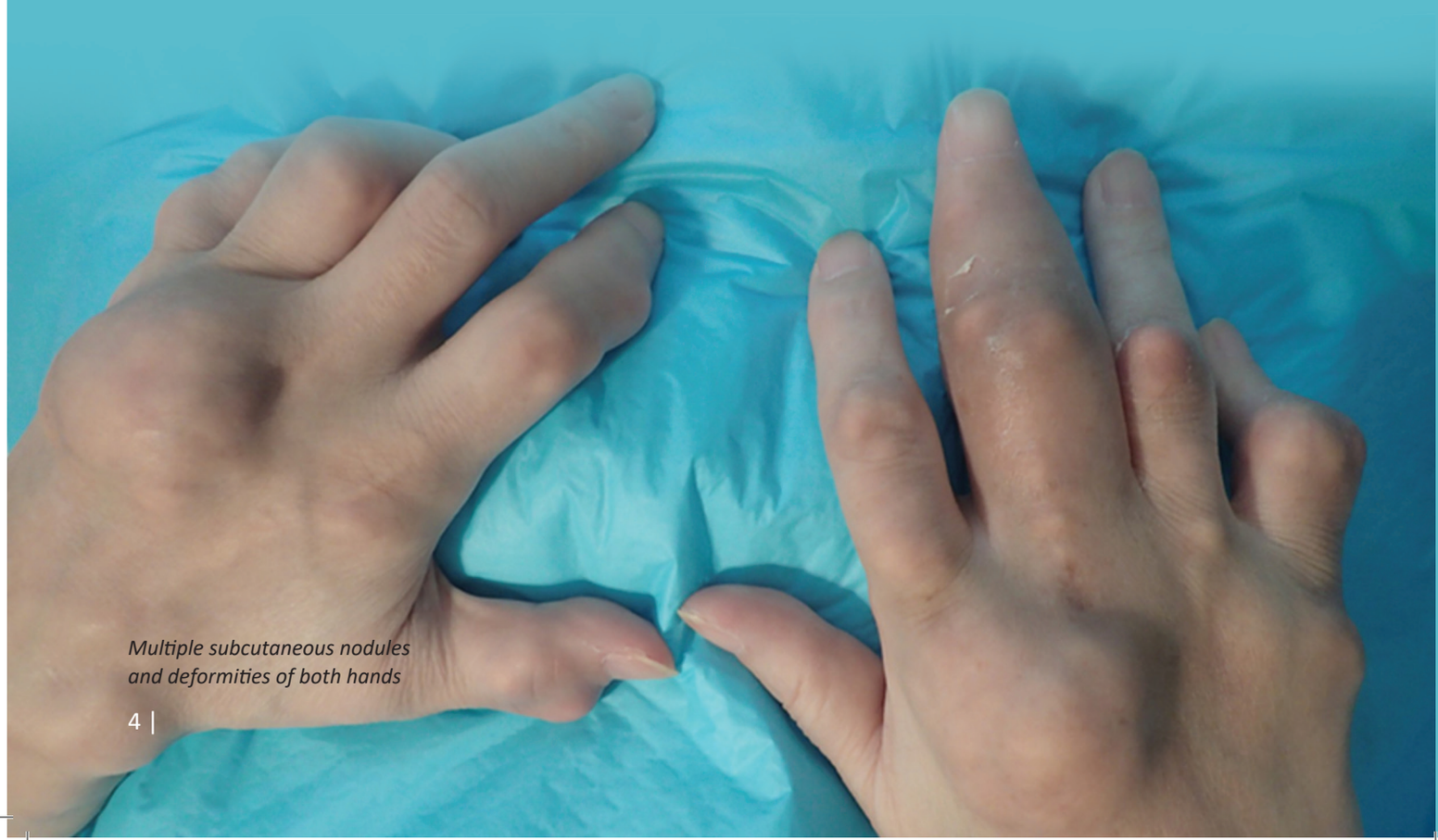
BMJ

A 56 year old man presented with multiple subcutaneous nodules over his body and deformities of both hands and feet. He had a seven year history of chronic peripheral polyarthritis (suspected to be rheumatoid arthritis) but had been reluctant to take antirheumatic therapy and did not attend clinic appointments. He consumed 40-60 g (5-7 units) of alcohol a day.

Examination revealed asymmetrical elastic, hard, painless, and partly ulcerated subcutaneous nodules around articular structures, tendons, and bursas. The nodules restricted extension of the left forefinger and left knee.

Plain joint radiography of the fingers and toes showed widespread destructive arthritis with joint dislocation, ankylosis, and well defined, punched out marginal erosions.

Ultrasound of the nodules, and of the finger, knee, and toe joints revealed hyperechoic linear densities over joint cartilage, hyperechoic spots in the synovium, and hypoechoic masses with hyperechoic spots.



Multiple subcutaneous nodules and deformities of both hands

Questions

1. What is the most likely diagnosis?
2. How is this condition confirmed?
3. What are the treatment options for this condition?

Answers

1. What is the most likely diagnosis?

Tophaceous gout.

Chronic enlargement of generalised subcutaneous elastic nodules in someone with destructive arthritis and high alcohol intake is suggestive of tophaceous gout. Joint involvement is asymmetric and asynchronic.

Raised serum urate is typical for tophaceous gout.

On ultrasound, the double contour sign (hyperechoic linear density over the surface of joint cartilage) and monosodium urate deposits (hyperechoic spots and masses) in the synovium are characteristic of tophaceous gout.

On radiography, punched out marginal erosions (also known as overhanging edges) are characteristic of chronic gout.

Rheumatoid arthritis is less likely in this patient because of his sero-negativity and polyarthritis with asymmetry and asynchrony.

2. How is this condition confirmed?

The diagnosis is usually clinical, but evidence of monosodium urate crystal deposition can be confirmed by dual energy computed tomography and magnetic resonance imaging. Monosodium urate crystals in tophus aspirates provides a definitive diagnosis.

3. What are the treatment options for this condition?

- Prompt urate lowering therapy. Febuxostat was the most effective.
- Non-steroidal anti-inflammatory drugs and colchicine to prevent gout flares during urate lowering therapy.
- Weight reduction with dietary changes, moderation of alcohol consumption, and avoidance of medications that induce hyperuricaemia, such as diuretics and low dose aspirin.
- Consider surgery for cosmetic reasons, or in cases complicated by soft tissue infection, nerve compression, joint deformity, and severe pain despite urate lowering therapy.

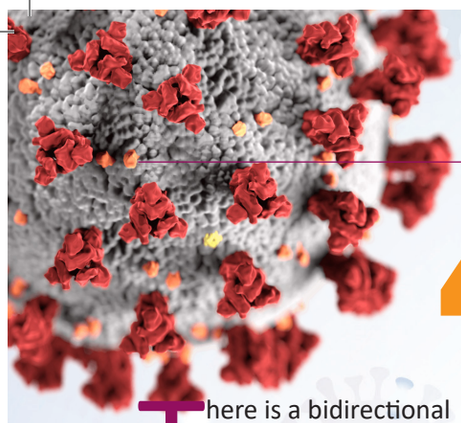
Learning points

- Clinical manifestations of gout include inflammatory arthritis with recurrent flare, chronic arthropathy, tophaceous deposits, urate nephrolithiasis, and chronic nephropathy.
- The European League Against Rheumatism recommends achieving a serum urate level <5 mg/dL to prevent progression of gouty complications, including tophi.

Patient outcome

We diagnosed tophaceous gout and initially administered allopurinol and analgesics. However, the patient developed a rash induced by the allopurinol, and we changed to febuxostat. We also advised alcohol cessation and offered social assistance.

His serum urate level normalizedand the tophi regressed. Future surgical management of the tophi in the involved joints will be considered if the functional joint disability remains after continued urate lowering therapy.



4 New-Onset Diabetes in Covid-19

There is a bidirectional relationship between Covid-19 and diabetes. On the one hand, diabetes is associated with an increased risk of severe Covid-19. On the other hand, new-onset diabetes and severe metabolic complications of preexisting diabetes, including diabetic ketoacidosis and hyperosmolarity for which exceptionally high doses of insulin are warranted, have been observed in patients with Covid-19.These manifestations of diabetes pose challenges in clinical management and suggest a complex pathophysiology of Covid-19–related diabetes.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes Covid-19, binds to angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed in key metabolic organs and tissues, including pancreatic beta cells, adipose tissue, the small intestine, and the kidneys.Thus, it is plausible that SARS-CoV-2 may cause pleiotropic alterations of glucose metabolism that could complicate the pathophysiology of preexisting diabetes or lead to new mechanisms of disease.

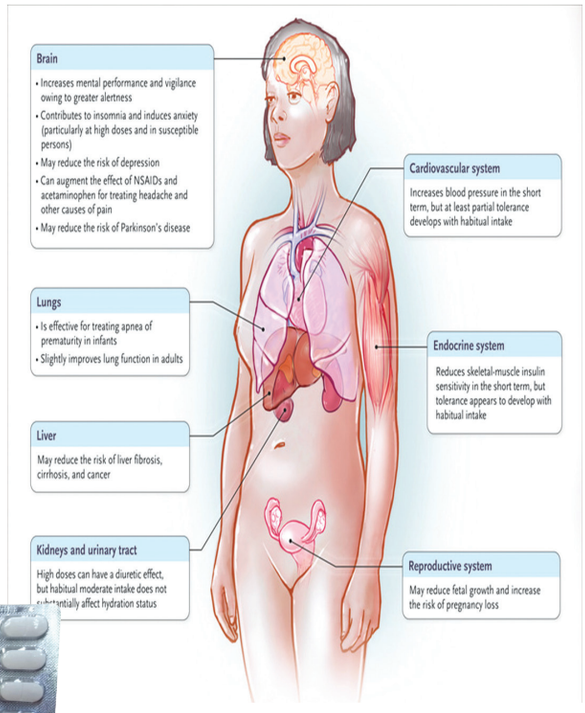
There are also several precedents for a viral cause of ketosis-prone diabetes, including other coronaviruses that bind to ACE2 receptors.Greater incidences of fasting glycemia and acute-onset diabetes have been reported among patients with SARS coronavirus 1 pneumonia than among those with non-SARS pneumonia.

5 Coffee, Caffeine and Health

Coffee and tea are among the most popular beverages worldwide and contain substantial amounts of caffeine, making caffeine the most widely consumed psychoactive agent.

A variety of plants contain caffeine in their seeds, fruits, and leaves. Besides coffee and tea, these plants include cacao beans (an ingredient of chocolate), yerba matte leaves (used to herbal tea) and guarana berries (used in beverages and supplements).

BENEFICIAL EFFECTS ON COGNITIVE PERFORMANCE AND PAIN.



6 Fasting Diet

The 5:2 intermittent fasting (IF) diet, more commonly referred to simply as the 5:2 diet, has become a popular approach to eating in recent years. Studies have shown that the diet helps with weight loss and may also reduce insulin resistance, both of which are of particular interest for many people with type 2 diabetes or borderline diabetes. One reason for the popularity of the diet is that it allows a certain amount of flexibility, in comparison to low calorie diets, on most days of the week. Many people use fasting alongside a low carb diet.

THEORY BEHIND THE DIET

The idea of the diet is that short periods of fasting prompt the body to repair damage but not enter a starvation mode of conserving energy. Whilst the theory has yet to be conclusively proved, clinical studies have shown promising results for the diet, however it has only been examined over relatively short time spans, of less than a year. There are several ways that intermittent fasting can be used to manage blood glucose levels, however this guide focuses on the 5:2 approach.

HOW THE 5:2 DIET WORKS

The 5:2 intermittent fasting diet is based on a simple idea. 5 days a week you stick to meeting the daily calorie intake advised for people of a healthy weight, that being:

- 2,500 kcal per day for men
- 2,000 kcal per day for women

For the other 2 days each week, the diet stipulates that you have only around 25% of the values above, which is equal to:

- 600 kcal on these days for men
- 500 kcal on these days for women

The fasting days can be taken at any time during the week as long as you do not take 2 fasting days consecutively.

BENEFITS OF THE 5:2 DIET

Clinical studies have shown that the benefits of intermittent fasting are largely similar to those of a calorie restricted diets . The most commonly reported benefits among people from following the 5:2 diet:

- Weight loss
- Decreased levels of triglycerides and LDL cholesterol
- Reduced blood pressure

- A reduction in insulin resistance

Research has shown that periods of fasting can help to improve life expectancy and decrease risks of diseases including nerve disorders, Alzheimer's disease and cancer. However, whether these benefits apply to a 5:2 fasting diet cannot be confirmed as long term clinical studies have yet to be performed.

IS THE 5:2 FAST DIET SAFE FOR DIABETES?

Whilst shorter term studies have displayed promise for intermittent fasting diets, long-term safety of the 5:2 diet is yet to be determined. As with any diet plan, you should always consult your GP or diabetes health team before making any significant changes to your diet as they could affect blood glucose levels or impact on your medication.

TYPE 2 DIABETES AND THE 5:2 FAST DIET

The fact that intermittent fasting shows evidence of improving insulin sensitivity may be an attractive option for people with a BMI over 25, borderline diabetes (prediabetes) or with type 2 diabetes but not on blood sugar-lowering medications. The diet may be good for people who can handle single days of significantly restricted calorie intake in preference to modest calorie restriction every day. On fasting days, the body will be forced to use stored energy from the body, fat and stored sugar (glycogen), which can help with weight loss and may improve blood glucose and cholesterol levels. If you are on insulin, or hypo causing medication, such as sulphonylureas or glinides, an intermittent fasting could significantly increase the risk of hypos. Your doctor should advise you on whether the diet is appropriate.

TYPE 1 DIABETES AND INTERMITTENT FASTING

If you have type 1 diabetes, following a 5:2 diet could make diabetes management more difficult to achieve and could significantly increase the risk of hypoglycemia .

HOW TO FOLLOW THE 5:2 DIET

Depending on your outlook, the 5:2 diet may be seen as more or less practical than a continuously reduced calorie diet. The benefit being that on most days you needn't consume less than the daily recommended calorie limit. However, some people may find that calorie intakes of 500 or 600 calories a day are too low to be practical. For best results, it's recommended to follow basic healthy eating rules, such as having a good intake of vegetables, fruit, and limiting intake of processed foods where possible. During the fasting days, you will need to rely on very low calorie meals to stay within the daily 500 or 600 calorie counts.

5:2 DIET FASTING DAY MEAL IDEAS

An example of good meal picks on fasting days include those based low fat foods such as:

- Eggs (65 kcal per medium egg)
- Grilled chicken breast without the skin (190 kcal per 100g)
- Prawns (105 kcal per 100g)
- Non-battered white fish (135 kcal per 100g)
- Cucumber (15 kcal per 100g)
- Celery (20 kcal per 100g)
- Bell pepper (26 kcal per 100g)

Liver Fat and Cardiometabolic Risk Factors Among School-Age Children

- The development of cardiometabolic risk factors in school-age children was evaluated based on the presence of liver fat. Liver fat was determined by MRI imaging, and nonalcoholic fatty liver disease (NAFLD) was present in individuals with ≥5.0% liver fat fraction.
- Compared with individuals with ≤2.00% liver fat, individuals with NAFLD were already at higher risk of the development of cardiometabolic risk factors, such as insulin resistance in childhood.

BACKGROUND AND AIMS

Nonalcoholic fatty liver disease is a major risk factor for cardiometabolic disease in adults. The burden of liver fat and associated cardiometabolic risk factors in healthy children is unknown. In a population-based prospective cohort study among 3,170 10-year-old children, we assessed whether both liver fat accumulation across the full range and nonalcoholic fatty liver disease are associated with cardiometabolic risk factors already in childhood.

APPROACH AND RESULTS

Liver fat fraction was measured by magnetic resonance imaging, and nonalcoholic fatty liver disease was defined as liver fat fraction ≥5.0%. We measured body mass index, blood pressure, and insulin, glucose, lipids, and C-reactive protein concentrations.

CONCLUSIONS

Higher liver fat is, across the full range and independently of body mass index, associated with an adverse cardiometabolic risk profile already in childhood. Future preventive strategies focused on improving cardiometabolic outcomes in later life may need to target liver fat development in childhood.

Lowering of Hemoglobin A1C and Risk of Cardiovascular Outcomes

Journal of Diabetes and Its Complications

This study examined the association between the magnitude of reduction in HbA1c in type 2 diabetes (T2D) patients and cardiovascular outcomes for sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1(GLP1) agonists, and dipeptidyl peptidase-4 (DPP4) inhibitors. Within individual medication classes, each additional 0.5% reduction in HbA1c in the active drug arm, relative to placebo, was associated with a lower incidence of cardiovascular events for GLP1 agonists but not for SGLT2 inhibitors or DPP4 inhibitors.

The results of this study further support the idea that reducing cardiovascular risk in Type 2 Diabetes is partly explained by a reduction in HbA1c, although this was seen with only one class of antidiabetic medication(GLP1) in this study.

Risk of Anemia With Metformin Use in Type 2 Diabetes

Hemoglobin and hematocrit decreased within 6 months of initiation of metformin.

In another RCT, hemoglobin declined by 3 years in the metformin group in comparison with other treatments. In the observational study, each 1 g/day of metformin use was associated with a 2% higher annual risk of anemia.

- In persons with type 2 diabetes, use of metformin is associated with early risk of anemia. The time course suggests that vitamin B12 deficiency is unlikely the sole cause.

OBJECTIVE

To evaluate the association between metformin use and anemia risk in type 2 diabetes, and the time-course for this, in a randomized controlled trial (RCT) and real-world population data.

RESEARCH DESIGN AND METHODS

Anemia was defined as a hemoglobin measure of <11 g/dL.

CONCLUSIONS

Metformin use is associated with early risk of anemia in individuals with type 2 diabetes, a finding consistent across two RCTs and replicated in one real-world study. The mechanism for this early fall in hemoglobin is uncertain, but given the time course, is unlikely to be due to vitamin B12 deficiency alone.

Research

Preterm delivery and long term mortality in women: national cohort and co-sibling study

BMJ 2020; https://doi.org/10.1136/bmj.m2533 (Published 19 August 2020)Cite this as: BMJ 2020;370:m2533

Abstract

Objectives To examine the long term mortality associated with preterm delivery in a large population based cohort of women, and to assess for potential confounding by shared familial factors.

Implications

Premature delivery should now be recognised as a risk factor for early mortality in women. Medical records and history taking should routinely include reproductive history that covers preterm delivery and other complications of pregnancy. Women with a history of preterm delivery need long term follow-up for recommended screenings to facilitate detection and treatment of chronic disorders associated with early mortality, including cardiovascular, neoplastic, and metabolic disease. Better access to high quality preconception and prenatal care should also be a public health priority to help reduce preterm delivery

Conclusions

This large national cohort study suggested that preterm and early term delivery were independent risk factors for premature mortality from several major causes, and that the associated risks persist for up to 40 years later. Women who deliver prematurely need long term clinical follow-up for detection and treatment of chronic disorders associated with early mortality.

What is already known on this topic

- Nearly 11% of all deliveries worldwide occur preterm (gestational age <37 weeks)
- Women who deliver preterm have been reported to have increased future risks of developing heart disease and other cardiometabolic disorders, but little is known about their long term mortality risks

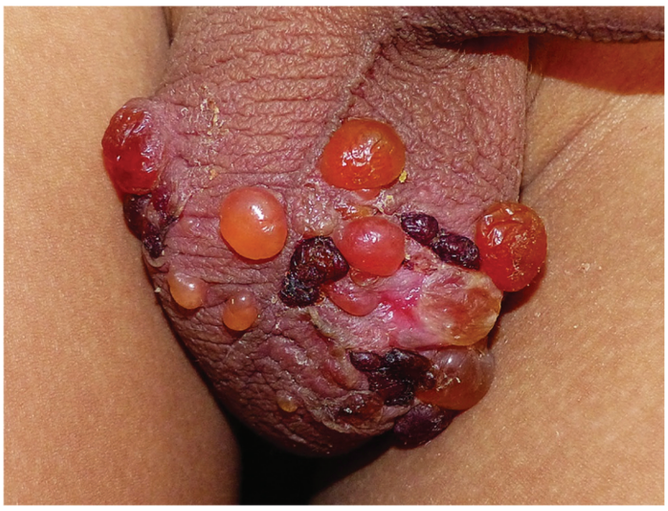
What this study adds

- In a large national cohort, preterm and early term delivery were independent risk factors for premature mortality in women up to 40 years later
- These findings were not explained by shared genetic or early life environmental factors in families
- Women who deliver prematurely need long term clinical follow-up for detection and treatment of chronic disorders associated with early mortality

Are Smartwatches and Mobile Phones Safe for Patients With Cardiovascular Implantable Electronic Devices?

- Because of the increasing use of smartwatches and mobile phones combined with concerns that electromagnetic interference can cause problems for patients with cardiovascular implantable electronic devices (CIEDs), this study examined the effects of a mobile phone (iPhone 6) and a smartwatch (Apple Watch A1553) on implanted devices in 148 patients. The smartwatch did not cause any effects on CIEDs or on telemetry. Although the smartphone caused interference with telemetry in 14% of patients, it generally did not cause interference with CIEDs, with only a single case noted.
- Based on these data, the contemporary smartwatch and mobile phone tested are unlikely to cause problematic interference with CIEDs, but clinicians should be aware that they may affect telemetry.

IMAGE CHALLENGE



The correct answer is linear IgA bullous dermatosis. The diagnosis was confirmed with biopsy and histopathological testing showing subepidermal blisters that contained eosinophilic and neutrophilic infiltrate and direct immunofluorescence antibody staining showing a linear band of IgA deposition along the dermoepidermal junction.

1. *Fixed drug eruption8%*
2. *Linear IgA bullous dermatosis42%*
3. *Dermatitis herpetiformis13%*
4. *Cutaneous bullous lupus13%*
5. *Bullous impetigo*

Summarised / Edited for Internal Circulation:

GLOCARE LABS PVT LTD

Clinical Research Organisation

BIOANALYTICAL UNIT:
2A, 3rd FL, Ganga Nagar, 4th Street, Kodambakkam, Chennai - 600 024, INDIA.
Tel: +91-44-24726001
Fax: +91-44-24726002

CLINICAL UNIT:
No. 37, BLN Prasad Nagar, V.O.C. Street, Kaikankuppam Road, Valasaravakkam, Chennai - 600 087, INDIA.
Ph: +91-44-4857 3985 Email: md@glocarelabscro.com
Website: www.glocarelabscro.com