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with increased NLR exacerbates the virus-induced inflammatory “storm”, possibly through the hepatic release of several proinflammatory cytokines, thereby contributing mechanistically to severe COVID-19 illness. However, further studies in larger Asian and non-Asian cohorts of COVID-19 patients are needed to better elucidate the link between MAFLD and COVID-19 severity.

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Author contributions

Ming-Hua Zheng contributed to the study concept, design and study supervision; Xiao-Bo Wang, Hua-Dong Yan, Qing-Feng Sun, Ke-Hua Pan, Kenneth I. Zheng, and Yong-Ping Chen all focused on the acquisition of data; Giovanni Targher contributed to the analysis and interpretation of data, and drafting of the manuscript; Alessandro Mantovani focused on both the analysis and interpretation of data and critical revision of the manuscript; Christopher D. Byrne, Mohammed Eslam, and Jacob George all contributed to the latter only.

Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.diabet.2020.06.001.

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Three alternative ways to screen for hyperglycaemia in pregnancy during the COVID-19 pandemic

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In 2010, the French-speaking Society of Diabetes (SFD; Société Francophone du Diabète) and French National College of Obstetricians and Gynaecologists (CNGOF) proposed an expert consensus on screening and caring for hyperglycaemia in pregnancy (HIP) in France. They recommended selective screening based on fasting
Fig. 1. French-speaking Society of Diabetes (SFD) recommendations for screening for hyperglycaemia in pregnancy before and during the COVID-19 pandemic: (A) current recommendations; and (B) alternative proposed during the pandemic. Plasma glucose values: 5.1 mmol/L = 92 mg/dL; 7.0 mmol/L = 126 mg/dL; 8.5 mmol/L = 153 mg/dL; 10.0 mmol/L = 180 mg/dL; HbA1c = 5.7% = 39 mmol/mol; 6.5% = 48 mmol/mol. FPG: fasting plasma glucose; G1 h/G2 h: plasma glucose at 1 h/2 h after 75-g oral glucose tolerance test; GDM: gestational diabetes mellitus; HbA1c: glycated haemoglobin; WG: weeks of gestation.
plasma glucose (FPG) measurement at the time of booking, followed by a 75-g oral glucose tolerance test (OGTT) at 24–28 weeks of gestation if the initial FPG result was normal. Gestational diabetes mellitus (GDM) and diabetes in pregnancy (DIP) were both defined according to International Association of Diabetes and Pregnancy Study Groups (IADPSG)/World Health Organization (WHO) criteria (Fig. 1A) [1].

In France, to maintain social distancing and self-isolation during the COVID-19 pandemic, some pathology collection centres have decided not to accommodate patients for the 2-h period required to perform an OGTT. In addition, some women do not wish to undergo the test. However, this decision is highly dependent on the region and hospital and/or on city structure. Nevertheless, the challenge has been to minimize the risks of COVID-19 infection and HIP-related complications. Given the latter situation, screening is still necessary and, therefore, the present authors have considered this issue on behalf of the SFD and CNGOF.

In the context of the COVID-19 pandemic, there is a need to:

- limit the number of screening tests for HIP;
- find alternate ways to screen for HIP when it appears to be neither sustainable nor safe to perform an OGTT.

Considering the first point, a recent French observational study found that selective screening was able to identify 84.6% of the women with HIP and also that women with HIP, but no risk factors, had a good prognosis [2]. Thus, selective screening is still recommended.

Screening tests are chosen for their high sensitivity, which may nonetheless be associated with low specificity and a high number of false-positive results. Any alternative to OGTT should minimize the possibility of missed HIP cases, particularly in women at high risk of complications. However, no single test can replace the OGTT in diagnosing GDM. The Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study showed that 50% of GDM cases, according to IADPSG criteria, were based on plasma glucose measurements at 1 h and/or 2 h after OGTT when FPG levels were normal [3]. Thus, FPG measurement alone does not appear to be sensitive enough.

The sensitivity of HbA1c levels at 24–28 weeks of gestation is low for detecting HIP, as defined by IADPSG criteria: it is only 5% for HbA1c ≥ 5.7% (39 mmol/mol) and 9% for HbA1c ≥ 5.9% (41 mmol/mol) [4]. The Royal College of Obstetricians and Gynaecologists recently reported unpublished data from two studies (http://2020-04-09-guidance-for-maternal-medicine-services-in-the-evolving-coronavirus-covid-19-pandemic.pdf) of the performance of HbA1c alone or in combination with FPG measurement to diagnose HIP. In a meta-analysis of 17 studies, a second/third trimester HbA1c cut-off value of ≥ 5.7% (39 mmol/mol) had high specificity [0.90; 95% confidence interval (CI): 0.70–0.95], but poor sensitivity for HIP detection (36%; 95% CI: 23–52). Therefore, HbA1c measurement alone is not sufficient.

In addition, a combined approach using both HbA1c and FPG measurement was evaluated in the Pregnancy and Infant Development (PRIDE) Study cohort (4303 women): HbA1c levels ≥ 5.7% (39 mmol/mol) and/or FPG levels ≥ 92 mg/dL had a detection rate of 51% for HIP, as defined by UK National Institute for Health and Care Excellence (NICE) criteria, and a 12% rate of false-positive cases. Moreover, HbA1c levels have been reported to be significantly associated with adverse pregnancy outcomes, including large-for-gestational-age (LGA) infants [5], caesarean sections [5], hypertensive disorders in pregnancy [5], preterm delivery [4], neonatal hyperbilirubinaemia [4] and neonatal asphyxia [4]. Thus, a high HbA1c level can identify those women who are at highest risk of adverse events.

Considering these data, we recommend the following pragmatic approach (Fig. 1B):

- at the time of booking, continue selective screening with FPG measurement;
- at 24–28 weeks of gestation, if FPG levels were < 92 mg/dL during early pregnancy, then it may be necessary to consider both FPG and HbA1c values as an alternative to OGTT [women with FPG ≥ 126 mg/dL or HbA1c ≥ 6.5% (48 mmol/mol) should be considered as having DIP; women with either FPG at 92–125 mg/dL or HbA1c of 5.7–6.4% should be considered as having GDM; and women with FPG < 92 mg/dL and HbA1c < 5.7% (39 mmol/mol) should be considered normal];
- in addition, at any time during pregnancy, women with high clinical suspicion of diabetes, LGA fetuses or polyhydramnios on ultrasound should also be tested.

Where permitted by local organizations and when there are no specific challenges for either patients or laboratories, it is recommended to continue the usual routine screening (Fig. 1A). However, in the absence of additional evidence, we recommend that this guidance be followed only for the duration of the COVID-19 pandemic, with a return back to the usual French recommended screening procedure when it appears to be safe and feasible to do so.

Disclosure of interest

The authors declare that they have no competing interest.

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