Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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.

Funding Sources

MHZ is supported by grants from the National Natural Science Foundation of China (81500665). CDB is supported in part by the Southampton NIHR Biomedical Research Centre (IS-BRC-20004), UK. GT is supported in part by grants from the School of Medicine, University of Verona, Verona, Italy.

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 for important intellectual content, while 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.

References

[1] Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. J Med Virol 2020. http://dx.doi.org/10.1002/jmv.25819 [Epub ahead of print].

[2] Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. J Hepatol 2020. http://dx.doi.org/10.1016/j.jhep.2020.03.039 [Epub ahead of print; pii: S0168-8278(20)30201-4].

[3] Alkhouri N, Morris-Stiff G, Campbell C, Lopez R, Tamimi TA, Yerian L, et al. Neutrophil to lymphocyte ratio: a new marker for predicting steatohepatitis and fibrosis in patients with non-alcoholic fatty liver disease. Liver Int 2012;32:297–302.

[4] Peng Y, Li Y, He Y, Wei Q, Xie Q, Zhang L, et al. The role of neutrophil to lymphocyte ratio for the assessment of liver fibrosis and cirrhosis: a systematic review. Expert Rev Gastroenterol Hepatol 2018;12:503–13.

[5] Targher G, Mantovani A, Byrne CD, Wang XB, Yan HD, Sun QF, et al. Risk of severe illness from COVID-19 in patients with metabolic dysfunction-associated fatty liver disease and increased fibrosis scores. Gut 2020. http://dx.doi.org/10.1136/gutjnl-2020-321611 [Online ahead of print; gutjnl-2020-321611].

[6] National Health Commission & State Administration of Traditional Chinese Medicine. Diagnosis and treatment protocol for novel coronavirus pneumonia (trial version 7); 2020 [EB/OL; 2020.03.03].

[7] Liu Y, Du X, Chen J, Jin Y, Peng L, Wang HHX, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalised patients with COVID-19. J Infect 2020. http://dx.doi.org/10.1016/j.jinf.2020.04.002 [pii: S0163-4453(20)30208-5; Epub ahead of print].

G. Targher[a,*], A. Mantovani[a], C.D. Byrne[b], X.-B. Wang[c], H.-D. Yan[d], Q.-F. Sun[e], K.-H. Pan[f], K.I. Zheng[g], Y.-P. Chen[g,h], M. Eslam[i], J. George[i], M.-H. Zheng[g,h,j,**]

[a]*Department of Medicine, Section of Endocrinology, Diabetes and Metabolism, University and Azienda Ospedaliera Universitaria Integrata of Verona, Piazzale Stefani 1, 37126 Verona, Italy*
[b]*Southampton National Institute for Health Research Biomedical Research Centre, University Hospital Southampton, Southampton General Hospital, Southampton, UK*
[c]*Department of Critical Care Medicine, Wenzhou Central Hospital, Wenzhou, China*
[d]*Department of Hepatology, Key Laboratory of Diagnosis and Treatment of Digestive System Tumours of Zhejiang Province, Hwamei Hospital, Ningbo No. 2 Hospital, University of Chinese Academy of Sciences, Ningbo, China*
[e]*Department of Infectious Diseases, Ruian People's Hospital, Wenzhou, China*
[f]*Department of Radiology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China*
[g]*Department of Hepatology, MAFLD Research Centre, the First Affiliated Hospital of Wenzhou Medical University, No. 2, Fuxue Lane, Wenzhou 325000, China*
[h]*Institute of Hepatology, Wenzhou Medical University, Wenzhou, China*
[i]*Storr Liver Centre, Westmead Institute for Medical Research, Westmead Hospital and University of Sydney, Sydney, Australia*
[j]*Key Laboratory of Diagnosis and Treatment for The Development of Chronic Liver Disease in Zhejiang Province, Wenzhou, China*

*Corresponding author at: Department of Medicine, Section of Endocrinology, Diabetes and Metabolism, University and Azienda Ospedaliera Universitaria Integrata of Verona, Piazzale Stefani 1, 37126 Verona, Italy**Co-corresponding author at: Department of Hepatology, MAFLD Research Centre, the First Affiliated Hospital of Wenzhou Medical University, No. 2, Fuxue Lane, Wenzhou 325000, China
E-mail addresses: giovanni.targher@univr.it (G. Targher)., zhengmh@wmu.edu.cn (M. Zheng).

Received 13 May 2020
Received in revised form 25 May 2020
Accepted 1st June 2020
Available online 4 June 2020

https://doi.org/10.1016/j.diabet.2020.06.001

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

ARTICLE INFO

Keywords:
Hyperglycemia in pregnancy
COVID 19 pandemic
Gestational diabetes

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

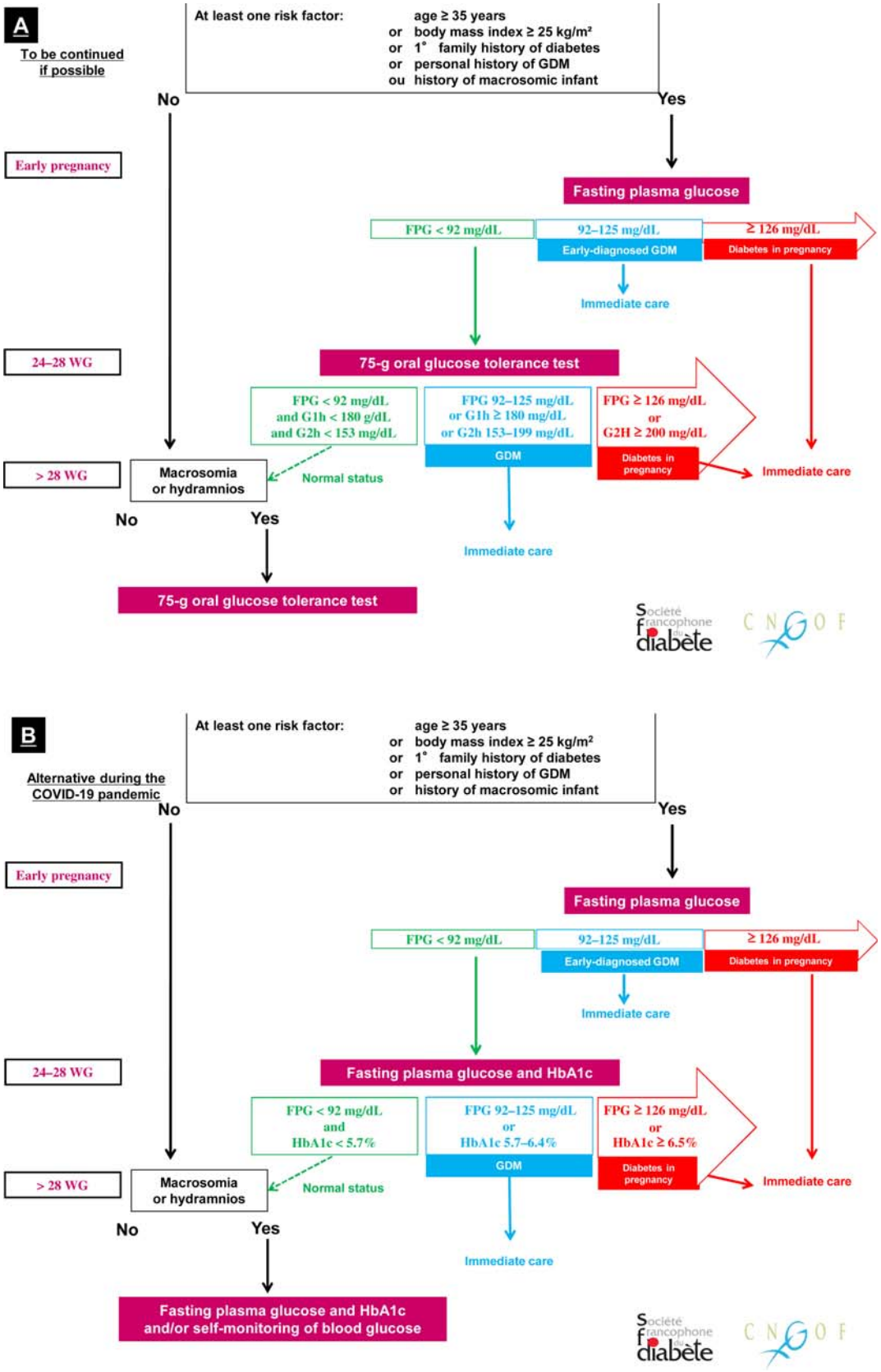

Fig. 1. French-speaking Society of Diabetes (SFD) recommendations for screening for hyperglycaemia in pregnancy before and during the COVID-19 pandemic: (A) current recommendations; and (B) alternative proposed during the pandemic. Plasma glucose values: 5.1 mmol/L = 92 mg/dL; 7.0 mmol/L = 126 mg/dL; 8.5 mmol/L = 153 mg/dL; 10.0 mmol/L = 180 mg/dL; HbA_{1c}: 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; HbA_{1c}: 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 HbA_{1c} levels at 24–28 weeks of gestation is low for detecting HIP, as defined by IADPSG criteria: it is only 5% for $HbA_{1c} \geq 5.7\%$ (39 mmol/mol) and 9% for $HbA_{1c} \geq 5.9\%$ (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 HbA_{1c} alone or in combination with FPG measurement to diagnose HIP. In a meta-analysis of 17 studies, a second/third trimester HbA_{1c} cut-off value of $\geq 5.7\%$ (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, HbA_{1c} measurement alone is not sufficient.

In addition, a combined approach using both HbA_{1c} and FPG measurement was evaluated in the Pregnancy and Infant Development (PRIDE) Study cohort (4303 women): HbA_{1c} levels $\geq 5.7\%$ (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, HbA_{1c} 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 HbA_{1c} 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 HbA_{1c} values as an alternative to OGTT [women with FPG ≥ 126 mg/dL or $HbA_{1c} \geq 6.5\%$ (48 mmol/mol) should be considered as having DIP; women with either FPG at 92–125 mg/dL or HbA_{1c} of 5.7–6.4% should be considered as having GDM; and women with FPG < 92 mg/dL and $HbA_{1c} < 5.7\%$ (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.

References

[1] Vambergue A. Expert consensus on gestational diabetes, mellitus. Diabetes Metab 2010;36(6 Pt 2):511.
[2] Cosson E, Vicaut E, Sandre-Banon D, Gary F, Pharisien I, Portal JJ, et al. Performance of a selective screening strategy for diagnosis of hyperglycaemia in pregnancy as defined by IADPSG/WHO criteria. Diabetes Metab 2019.
[3] Study Cooperative Research Group HAPO, Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991–2002.
[4] Ye M, Liu Y, Cao X, Yao F, Liu B, Li Y, et al. The utility of HbA_{1c} for screening gestational diabetes mellitus and its relationship with adverse pregnancy outcomes. Diabetes Res Clin Pract 2016;114:43–9.
[5] Sweeting AN, Ross GP, Hyett J, Molyneaux L, Tan K, Constantino M, et al. Baseline HbA1c to identify high-risk gestational diabetes:utility in early vs standard gestational diabetes. JCEM 2017;102:150–6.

A. Vambergue[a,i,*], S. Jacqueminet[b,i], M.-F. Lamotte[c,i]
F. Lamiche-Lorenzini[d,i], C. Brunet[e,i], P. Deruelle[f,j], C. Vayssière[g,j],
E. Cosson[h,i]
[a]*Endocrinology, Diabetology, Metabolism and Nutrition Department, Lille University Hospital, European Genomics Institute for Diabetes, University of Lille, France*
[b]*Diabetology Department, Cardiometabolism and Nutrition Institute (ICAN), AP-HP6, Hôpitaux Universitaires Pitié Salpêtrière–Charles Foix, 75013 Paris, France*
[c]*Nutrition, Endocrinology, Metabolic Diseases, Department ENDO, Assistance Publique Hôpitaux de Marseille (AP-HM), France*
[d]*CH Jura Sud, Lons-Le-Saunier, France*
[e]*Endocrinology Diseases Department, CHU Montpellier, France*

[f]*Department of Obstetrics and Gynecology, University Hospital of Strasbourg, France*
[g]*Department of Obstetrics and Gynecology, Paule de Viguier Hospital, CHU Toulouse, France, UMR 1027 Inserm, Team SPHERE, Toulouse III University, Toulouse, France*
[h]*AP-HP, Avicenne Hospital, Paris 13 University, Sorbonne Paris Cité, Department of Endocrinology-Diabetology-Nutrition, CRNH-IdF, CINFO, UMR U557 Inserm/U11125 INRAE/CNAM/Université Paris13, Unité de Recherche Epidémiologique Nutritionnelle, Bobigny, France*
[i]*Francophone Society of Diabetes (SFD), France*
[j]*French National College of Obstetricians and Gynecologists (CNGOF), France*

*Corresponding author at: CHRU de Lille, Endocrinology, Diabetology, Metabolism and Nutrition Department, 59000 Lille, France
E-mail address: anne.vambergue@chru-lille.fr (A. Vambergue).

Received 28 April 2020
Accepted 29 April 2020
Available online 6 May 2020

https://doi.org/10.1016/j.diabet.2020.04.003