and was revived by cardiopulmonary resuscitation then treated in the intensive care unit. Her plasma glucose level was 56.3 mmol/l (1,013 mg/dl) and HbA_{1c} was 6.5%. Serum and urinary C-peptide levels were very low (0.2 ng/ml and 3 μg/day, respectively). There was no increase in C-peptide following intravenous administration of 1 mg glucagon. She had no islet-associated autoantibodies (GAD antibody, islet cell antibody, or insulinoma-associated antigen-2 [IA-2] antibody. Her serum amylase was 7,492 IU/l (normal range 30–130). She had elevated lipase and trypsin levels (52 units/l [0–49] and 2,860 ng/ml [100–550], respectively). These findings were consistent with fulminant type 1 diabetes, and she was treated with intensive insulin therapy. The patient had HLA-A24, which is reported to be associated with β-cell destruction (9), and had a homozygous HLA-DR9-DQ3 haplotype, which is strongly associated with autoimmune (type 1A) diabetes (10).

After admission, she had persistent sinus tachycardia. Thirteen days after admission, an echocardiogram revealed paroxysmal atrial fibrillation. At that time, her thyroid hormones were elevated (fT3 10.4 pg/ml, fT4 4.4 ng/dl) and thyroid-stimulating hormone was suppressed (<0.03 μU/ml). Thyroid-stimulating hormone receptor antibody was negative, and a 99m-Tc–labeled thyroid scan revealed a decreased uptake (Tc RI uptake ratio 0.275% [normal range 0.4–3.0]). Thyroid-stimulating hormone measured at the previous clinic 1 day before her admission was within normal limits. Thus, the onset of fulminant type 1 diabetes and painless thyroiditis appeared to be simultaneous.

Cases of fulminant type 1 diabetes with thyroid disease or with thyroid-related antibody were previously reported (11,12), and these cases were suggested to have immunogenetic characteristics. Painless thyroiditis is also generally considered to be an autoimmune disorder (13). This case also suggests participation of autoimmune mechanisms at the onset of fulminant type 1 diabetes. On the other hand, the association of a viral infection cannot be excluded because of preceding symptoms of infection. In a nationwide survey (14), fulminant diabetes comprises ~20% of Japanese type 1 diabetes with ketosis or ketoacidosis at the onset. This new subtype, however, might be a heterogeneous entity. This is the first case of fulminant type 1 diabetes associated with simultaneous painless thyroiditis. It is useful to follow such cases to elucidate fulminant type 1 diabetes etiology, and further study is required to clarify its entity.

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References

1. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 21 (Suppl. 1):S5–S19, 1998
2. Imagawa A, Hanafusa T, Miyazawa J, Matsuzawa Y: A novel subtype of type 1 diabetes mellitus characterized by a rapid onset and an absence of diabetes-related antibodies. *N Engl J Med* 342:301–307, 2000
3. Imagawa A, Hanafusa T, Makino H, Miyagawa J-I, Juto P: High titres of IgA antibodies to enterovirus in fulminant type 1 diabetes. *Diabetologia* 48:290–293, 2005
4. Sekine N, Motokura T, Oki T, Umeda Y, Sasaki N, Hayashi M, Sato H, Fujita T, Kaneko T, Asano Y, Kikuchi K: Rapid loss of insulin secretion in a patient with fulminant type 1 diabetes mellitus and carbamazepine hypersensitivity syndrome. *JAMA* 285:1153–1154, 2001
5. Shimada A, Morimoto J, Kodama K, Oikawa Y, Irie J, Nakagawa Y, Narumi S, Saruta T: T-cell–mediated autoimmunity may be involved in fulminant type 1 diabetes (Letter). *Diabetes Care* 25:635–636, 2002
6. Shimada A, Oikawa Y, Shigihara T, Senda T, Kodama K: A case of fulminant type 1 diabetes with strong evidence of autoimmunity (Letter). *Diabetes Care* 25:1482–1483, 2002
7. Taniguchi T, Tanaka J, Seko S, Okazaki K, Okamoto M: Association of rapid-onset type 1 diabetes and clinical acute pancreatitis positive for autoantibodies to the exocrine pancreas (Letter). *Diabetes Care* 24:2156–2157, 2001
8. Taniguchi T, Okazaki K, Okamoto M, Seko S, Nagashima K, Yamada Y, Iwakura T, Seino Y: Autoantibodies against the exocrine pancreas in fulminant type 1 diabetes (Letter). *Pancreas* 30:191–192, 2005
9. Nakanishi K, Kobayashi T, Murase T, Nakatsuji T, Inoko H, Tsuji K, Kosaka K: Association of HLA-A24 with complete beta-cell destruction in IDDM. *Diabetes* 42:1086–1093, 1993
10. Imagawa A, Hanafusa T, Uchigata Y, Kanatsuka A, Kawasaki E, Kobayashi T, Shimada A, Shimizu I, Maruyama T, Makino H: Different contribution of class II HLA in fulminant and typical autoimmune type 1 diabetes mellitus. *Diabetologia* 48: 294–300, 2005
11. Sakaue S, Nagata M, Wakabayashi O, Honda T, Yoshimura H, Yamaguchi T, Nishimura M: A case of fulminant type 1 diabetes with elevated rheumatoid factor and the temporal presence of thyroid-stimulating hormone receptor antibody (Letter). *Diabetes Care* 25:935–936, 2002
12. Miura Y, Suzuki A, Sato I, Kato Y, Oiso Y: A case of fulminant type 1 diabetes with Grave's disease (Letter). *Diabetes Care* 25: 1894–1895, 2002
13. Dayan CM, Daniels GH: Chronic autoimmune thyroiditis. *N Engl J Med* 335:99–107, 1996
14. Imagawa A, Hanafusa T, Uchigata Y, Kanatsuka A, Kawasaki E, Kobayashi T, Shamada A, Shimizu I, Toyoda T, Maruyama T, Makino H: Fulminant type 1 diabetes: a nationwide survey in Japan. *Diabetes Care* 26:2345–2352, 2003

Recurrence of Diabetes After Diarrhea-Associated Hemolytic Uremic Syndrome

We read with interest the article by Suri et al. (1). In this article, we find a systematic review and meta-analysis of articles assessing diabetes during diarrhea-associated hemolytic uremic syndrome (D+HUS). The 21 included studies describe 49 children who developed diabetes during acute D+HUS. Long-term outcome was reported for 44 of 49 children: 13 of 34 survivors were left with persistent diabetes requiring insulin; 11 had persistent diabetes from the outset, while 2 redeveloped diabetes at 3 and 60 months after initial apparent recovery, respectively. The remaining 21 children were reported to have made a complete recovery from diabetes. However, follow-up was <12 months or not reported for these children.

We report a boy with relapse of diabetes after 82 months (6.8 years). This boy was hospitalized with severe D+HUS when he was 6 years old. During his stay in the intensive care unit, he developed hyperglycemia and was treated with insulin during 21 days. Eighty months later he presented with nose obstruction and headache and was diagnosed with sinusitis and polyposis nasi. He was treated with antibiotics, but the complaints persisted. Two months later, he was operated on (functional endoscopic sinus surgery), and postoperatively he received 2 mg betamethason for 5 days. On the 5th day, he presented in the emergency department with polyuria, polydipsia, and lethargy. His glycemia was 1,500 mg/dl, and his blood pH was 7.33. He was intravenously treated with insulin, and the corticosteroids were ceased.

To differentiate between type 1 diabetes, glucocorticoid-induced diabetes, and post-HUS diabetes, some additional blood tests were done. Pancreatic autoantibodies, including islet cell, insulin, GAD65, and insulinoma-associated protein 2 antibodies were all negative. Insulin was 4 mU/l for a glycemia of 1,453 mg/dl. After normalization of the glycemia, the boy was started on a basal-bolus regimen with insulin aspart and insulin glargine. Twenty months later, he still requires insulin ($0.5 \text{ units} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$) and has an HbA_{1c} of 6.8%.

Our report in which we describe a relapse of diabetes after 82 months confirms the conclusion of Suri et al. that survivors of D+HUS should have aggressive surveillance and treatment of hyperglycemia, not only in the acute phase but also in the long run.

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References

1. Suri RS, Clark WF, Barrowman N, Mahon JL, Thiessen-Philbrook HR, Rosas-Arellano MP, Zarnke K, Garland JS, Garg AX: Diabetes during diarrhea-associated haemolytic uremic syndrome. *Diabetes Care* 28:2556–2562, 2005

Maternal Age and Prevalence of Gestational Diabetes Mellitus

Maternal age is an established risk factor for gestational diabetes mellitus (GDM), but there is no consensus on the age above which there is significantly increased risk of GDM. In the literature, the lowest cutoff is ≥25 years, as recommended by the American Diabetes Association (1), but there are little data to support this recommendation. To determine the age threshold for increased risk of GDM, we have reviewed the prevalence of GDM, diagnosed by the World Health Organization criteria (2), in the singleton pregnancies managed in our department from 1998 to 2001. Data on maternal anthropometric parameters, parity status, and risk factors for GDM such as booking weight ≥70 kg, BMI ≥25 kg/m^2, chronic hypertension, significant medical history, and smoking, as well as risk factors identified in our population that included carrier of thalassemia trait (3) and HBsAg (4) and presence of iron deficiency anemia, which reduces the risk of GDM (5), were retrieved from a computerized database. The pregnancies were categorized according to maternal age, i.e., ≤20 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, and ≥40 years, for statistical analysis (SPSS for Windows version 11.0; SPSS, Chicago, IL) using the χ^2 test and Pearson's correlation. Multivariate analysis was used to determine the role of advancing maternal age adjusting for the other significant associated factors, and the adjusted relative risk and 95% CI was calculated for each age cohort with the 20–24 years cohort as the reference.

Of the 16,383 women managed in this period, 15,827 (96.6%) women continued their pregnancies beyond the first trimester, and the number (% of total) from the youngest to the oldest cohort were 318 (2.0%), 1,713 (10.8%), 4,446 (28.1%), 5,457 (34.5%), 3,279 (20.7%), and 614 (3.9%), respectively. There was a significant difference and positive correlation in the prevalence of GDM, increasing from 1.3, 2.5, 6.2, 10.3, 21.7, and 31.9%, respectively, from the youngest to the oldest cohort ($P < 0.001$). On multivariate analysis and adjusting for significant confounding factors that included weight ≥70 kg, BMI ≥25 kg/m^2, HBsAg carrier, thalassemia trait carrier, significant medical history, multiparity, smoker, and absence of iron deficiency anemia, the risk for the older cohorts was significantly increased as follows: 25–29 years, 2.59 (1.84–3.67); 30–34 years, 4.38 (3.13–6.13); 35–39 years, 10.85 (7.72–15.25); and ≥40 years, 15.90 (10.62–23.80). There was no significant difference for the <20 years cohort.

Our finding indicates that the risk of GDM becomes significantly and progressively increased from 25 years onwards. This supports the American Diabetes Association recommendation on the use of age ≥25 years as the cutoff for screening and the observation that maternal age ≥25 years is the factor most predictive of GDM (6). In clinical practice, maternal age of ≥25 years should be adopted instead of ≥35 years or 40 years as a risk factor for the development of GDM.

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References

1. American Diabetes Association: Gestational diabetes mellitus. *Diabetes Care* 27 (Suppl. 1): S88–S90, 2004
2. World Health Organization: *WHO Expert Committee on Diabetes Mellitus*. Geneva, World Health Org., 1980, p. 8–12 (Tech. Rep. Ser., no. 646)
3. Lao TT, Ho LF: α-Thalassaemia trait and gestational diabetes mellitus in Hong Kong. *Diabetologia* 44:966–971, 2001
4. Lao TT, Tse KY, Chan LY, Tam KF, Ho LF: HBsAg carrier status and the association between gestational diabetes with increased serum ferritin concentration in Chinese women. *Diabetes Care* 26:3011–3016, 2003
5. Lao TT, Ho LF: Impact of iron deficiency anemia on prevalence of gestaional diabetes mellitus. *Diabetes Care* 27:650–656, 2004
6. Danilenko-Dixon DR, Van Winter JT,