Gestational Diabetes and the New Screening Test’s Impact

Diabetes Gestacional e o Impacto do Actual Rastreio

Ana Catarina MASSA¹, Ricardo RANGEL², Manuela CARDOSO³, Ana CAMPOS¹
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ABSTRACT

Introduction: In 2011, a new screening test for gestational diabetes was introduced which allowed an earlier and larger diagnosis with the goal of reducing maternal and perinatal complications. The aim of our study was to evaluate the prevalence of gestational diabetes, compare maternal and perinatal outcomes with the previous and present screening tests and analyze postpartum screening results.

Material and Methods: Retrospective study of women with singletons and gestational diabetes diagnosed during 2009 (n = 223) and 2012 (n = 237), at Maternidade Dr. Alfredo da Costa, Portugal. Analysis of clinical charts and assessment of demographic data, medical and obstetric history, weight gain during pregnancy, gestational age at diagnosis, treatment regimens, neonatal outcomes and postpartum screening results, followed by comparison of these variables between the years of 2009 and 2012.

Results: In 2012, there was an increased gestational diabetes prevalence, lower weight gain during pregnancy (p < 0.001), more frequent use of pharmacological therapy (p < 0.001) and more diagnosed cases during first and second trimester (p < 0.001). As for neonatal outcomes, in this group, the medium weight at birth was significantly lower (p = 0.001) with a decrease of newborns great for gestational age (p = 0.002). Postpartum screening rate was similar among both groups but in 2012 there was an increase of normal results and a decrease of impaired fasting glucose.

Discussion: Tighter criteria of the current screening test resulted in reduction of the majority of gestational diabetes complications but raised new questions.

Conclusion: The introduction of the current screening test resulted in an increased prevalence, earlier diagnosis and reduction of macrosomia.

Keywords: Gestational Diabetes; Mass Screening.

RESUMO

Introdução: Em 2011, foi introduzido um novo rastreio para a diabetes gestacional que permitiu um diagnóstico mais precoce e de maior número de casos com o intuito de reduzir complicações maternas e perinatais. O objectivo deste estudo foi avaliar a prevalência da diabetes gestacional, comparar resultados obstétricos e perinatais do anterior e presente rastreio e os resultados e realização da prova de reclassificação pós-parto.

Material e Métodos: Estudo retrospectivo em gestações simples e diabetes gestacional diagnosticados em 2009 (n = 223) e 2012 (n = 237), vigiadas na Maternidade Dr. Alfredo da Costa, Portugal. Após consulta de processos clínicos procedeu-se à análise de características demográficas, história médica e obstétrica, aumento ponderal durante a gravidez, idade gestacional do diagnóstico, terapêutica utilizada, resultados perinatais e reclassificação pós-parto, seguida de comparação destas variáveis entre os anos de 2009 e 2012.

Resultados: Em 2012, houve maior prevalência de diabetes gestacional, ganho ponderal inferior (p < 0,001), maior recurso à terapêutica farmacológica (p < 0,001) e aumento dos casos diagnosticados no primeiro e segundo trimestre (p < 0,001). Relativamente aos resultados neonatais, o peso médio do recém-nascido ao nascer foi significativamente menor (p = 0,001) com diminuição dos recém-nascidos grandes para a idade gestacional (p = 0,002). A taxa de reclassificação pós-parto foi semelhante nos dois anos mas em 2012 houve um aumento dos resultados normais e diminuição das anomalias da glicemia em jejum.

Discussão: Critérios mais apertados do actual rastreio permitiram a redução da maioria das complicações da diabetes gestacional levantando novas questões.

Conclusão: A introdução do actual rastreio resultou num aumento de prevalência, diagnóstico mais precoce e redução da macrosomia.

Palavras-chave: Diabetes Gestacional; Rastreio.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of most common medical complications in pregnancy, with an increasing incidence over the last few years. It is defined as the intolerance to carbohydrate of variable intensity, first presenting or diagnosed in pregnancy, with 5 to 7% estimated prevalence and usually remitting upon delivery.¹⁻⁷

Several risk factors have been identified including advanced maternal age, ethnicity (Hispanic, Afro-American and Asian), high preconception body mass index (BMI), prior GDM or DM1 (type-1 diabetes mellitus) and a DM2 (type-2 diabetes mellitus) family history.⁵,⁶,⁸

Previous studies have shown an association between GDM and adverse outcomes (short and long-term). Gestational hypertensive disorders, such as pregnancy-induced hypertension (PIH) and pre-eclampsia (PE) and a risk of development of DM2 on average 22 to 28 years later,
are examples of maternal complications. Foetal outcomes include macrosomia, increase in caesarean delivery rate, shoulder dystocia, neonatal respiratory distress syndrome and metabolic complications.\textsuperscript{1,4,6}

In Portugal, from 2000 to 2010, the recommended GDM diagnosis was based on a two-step approach – initially, a screening 50 g oral glucose challenge testing during the 2nd and 3rd trimester or the first trimester if there were any risk factors, followed by a 100 g oral glucose diagnostic test upon a positive screening test.\textsuperscript{8}

The HAPO (Hyperglycaemia and Adverse Pregnant Outcomes) study has altered screening recommendations. This was a multi-centric study regarding the assessment of glucose tolerance between 24 and 32 weeks of pregnancy testing for fasting blood glucose ≥ 92 mg/dl during the first trimester or for a change in the result of the oral glucose tolerance test (OGTT 75 g – 0 h ≥ 92 mg/dL, 1 h ≥ 180 mg/dl, 2 h ≥ 153 mg/dl) as criteria for GDM diagnosis. It demonstrated a linear relationship between the levels of maternal blood glucose and maternal, foetal and perinatal morbidity.\textsuperscript{2} This screening test was first implemented in Portugal in 2011 and the timeframe between 24 and 28 weeks was recommended as most adequate in order to cover the highest number of diagnosed cases. It was supported by the Portuguese Directorate-General of Health (Direcção Geral de Saúde), the Portuguese Society of Endocrinology, Diabetes and Metabolism (Sociedade Portuguesa de Endocrinologia, Diabetes e Metabolismo), the Portuguese Society of Diabetology (Sociedade Portuguesa de Diabetologia), The Obstetrical and Maternal-fetal Medicine Society (Sociedade de Obstetricia e Medicina Materno-Fetal) as well as the Neonatology Section of the Portuguese Society of Pediatrics (Sociedade Portuguesa de Pediatria) aiming for very early diagnosis and for testing a higher number of pregnant mothers, thus reducing the hypertensive outcomes rate, macrosomia, caesarean delivery and shoulder dystocia rate through more rigorous monitoring of blood glucose and early therapy.\textsuperscript{1,4,7} This screening was also adopted by some International Societies, namely by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) and by the American Diabetes Association.\textsuperscript{3}

Every GDM sufferer should undergo a reclassification test by means of a 75 g OGTT 6-8 years after pregnancy –, with two glucose determinations: at 0 h (fasting) and at 2 h.\textsuperscript{6,7,8} The test is considered negative when the first level is below 110 mg/dL and the second is below 140 mg/dL. The criteria used to consider a postnatal reclassification test as normal or a fasting glucose disorder, impaired glucose tolerance or DM2 are shown in Table 1.\textsuperscript{7}

Our study aimed to compare the obstetric and perinatal outcomes of pregnant mothers who underwent the present and the previous screening test and to evaluate the results of postnatal reclassification of glucose tolerance (2009 vs. 2012). The GDM prevalence was also evaluated.

The timeframes chosen, 2009 and 2012, aimed to allow for the comparison of obstetric and perinatal outcomes between both screening methods: in 2009, based on a screening test and requiring confirmation with the diagnostic test; in 2012, with the current screening, where diagnosis only requires the presence of changes in the result of the screening test.

**MATERIAL AND METHODS**

A retrospective study was performed at the Maternidade Alfredo da Costa – tertiary perinatal centre, involving pregnant mothers with single pregnancies attending the Diabetes Outpatient and diagnosed with GDM, in 2009 and 2012. The following parameters were assessed:

- Patient's demographic characteristics: maternal age and preconception BMI;
- Obstetric history: parity, GDM and foetal macrosomia history;
- Family history of DM1 or DM2;
- The trimester corresponding to the GDM diagnosis, therapeutic measures (nutritional and/or pharmacological – insulin, metformin or both) and the HbA1c level in the first trimester;
- Weight increase and gestational hypertensive complications;
- Variables regarding delivery and the newborn (NB) child: gestational age (GA) at delivery, type of delivery (eutocic, dystocia and caesarean section), NB’s weight at birth, NB’s Apgar Score (AS), NB’s percentile at birth according to AS and gender, shoulder dystocia;
- Postnatal reclassification of glucose tolerance.

Data collection was based on clinical records. Twin pregnancies or with an unknown perinatal outcome were excluded from the study.

The statistical analysis used the SPSS 20.0\textsuperscript{8} version.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Fasting</th>
<th>2h upon glucose load</th>
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<tbody>
<tr>
<td>Normal</td>
<td>&lt; 110 mg/dL</td>
<td>AND</td>
</tr>
<tr>
<td>Impaired fasting glucose</td>
<td>≥ 110 mg/dL and &lt; 126 mg/dL</td>
<td>AND</td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td>&lt; 126 mg/dL</td>
<td>AND</td>
</tr>
<tr>
<td>Type-2 diabetes mellitus</td>
<td>≥ 126 mg/dL</td>
<td>OR</td>
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<td></td>
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<td>≥ 200 mg/dL</td>
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Table 1 – Reference levels for the reclassification test
through Chi-square test, Fisher’s exact test and Mann-Whitney’s test. A statistical significance level of $p \leq 0.05$ was used.

**RESULTS**

In 2009 and 2012, a total of 223 and 237 pregnant mothers, respectively attended the Diabetes Outpatient Department. Since 5,101 single deliveries were carried out in the Maternity (Maternidade Dr. Alfredo da Costa) in 2009 and 4,412 in 2012, GDM prevalence has increased by 22.8% in this time period, from 4.37% to 5.37%.

As regards patient’s demographic characteristics, obstetric and family history, both groups were similar (Table 2).

A lower weight increase was found in 2012 ($11.01 \pm 5.35$ vs. $8.97 \pm 6.44$, $p < 0.001$) and an increase in GDM cases were diagnosed in the first and second trimesters (T) (1st T – 1.8%, 2nd T – 26.5%, 3rd T – 71.7% vs. 1st T – 30.8%, 2nd T – 53.2%, 3rd T – 16%, $p < 0.001$). A higher use of pharmacological therapy associated to nutritional therapy was also found, when compared to the single use of the latter (16.1% vs. 38.8%, $p < 0.001$) (Table 3). As regards pharmacological therapy, while in 2009 only insulin was used (36 patients / 16%), in 2012, insulin was used in association with metformin (12 patients / 5%) as well as metformin alone (23 patients / 10%) or insulin alone (57 patients / 24%). However, the nutritional therapy alone remained as the most frequent therapy on both screenings (187 patients / 84% in 2009 vs. 145 patients / 61% in 2012).

There were no statistically significant differences regarding the average level of HbA1c in the third trimester ($5.39 \pm 1.0$ vs. $5.58 \pm 0.5$, $p > 0.05$) or the presence of hypertensive complications (Table 3).

As regards newborn outcomes, the average GA at birth, type of delivery and shoulder dystocia were similar in both groups. However, there was a trend towards a reduction in the number of caesarean sections with the current screening. In addition there was a reduction in the elective

<table>
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<tr>
<th>Table 2 – Demographic characteristics and obstetric and family history of our group of patients in 2009 and in 2012</th>
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<tr>
<td><strong>2009</strong> &lt;br&gt; &lt;sup&gt;(n = 223)&lt;/sup&gt;</td>
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<tr>
<td>Maternal age (years)</td>
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<tr>
<td>Parity</td>
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<tr>
<td>Nulliparous</td>
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<tr>
<td>Non-nulliparous</td>
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<tr>
<td>Preconception BMI (kg/m$^2$)</td>
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<tr>
<td>Diabetes in previous pregnancy</td>
</tr>
<tr>
<td>Foetal macrosomia</td>
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<td>Family history of diabetes</td>
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NS – not significant. BMI – body mass index.

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<th>Table 3 – Variables of pregnancy in 2009 and 2012</th>
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<tr>
<td><strong>2009</strong> &lt;br&gt; &lt;sup&gt;(n = 223)&lt;/sup&gt;</td>
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<tr>
<td>GA at the time of diagnosis, by trimester</td>
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<tr>
<td>1st T</td>
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<td>2nd T</td>
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<tr>
<td>3rd T</td>
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<tr>
<td>Weight gain (kg)</td>
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<td>HbA1c at 3rd trimester</td>
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<tr>
<td>Therapy</td>
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<tr>
<td>Nutritional</td>
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<td>Pharmacologic</td>
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<td>Hypertensive complications</td>
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caesarean rate due to an estimated weight above 4,000 g and in emergency caesarean rate due to dystocia. In addition, an increase in emergency caesarean section due to non-reassuring foetal status (NRFS) was found (Table 4).

Newborn’s weight at birth was significantly lower in 2012 than in 2009 (3,339.1 ± 524.5 vs. 3,163.1 ± 582.58, p = 0.001). Differences were also found when comparing appropriate for gestational age (AGA), small for gestational age (SGA) and large for gestational age (LGA) NB rates between 2009 and 2012 (p = 0.001). There was an increase in LGA NB rate (83% vs. 88%), in SGA NB (6% vs. 8%) and a reduction in the LGA NB rate (11% vs. 4%). However, only the latter was statistically significant (p = 0.002) (Table 5). Further studies with larger samples are required to confirm this tendency.

In 2009, an assessment of the relationship between insulin vs. nutritional therapy found that the former was significantly associated to a reduction in the NB’s weight percentile for the GA (insulin – eight LGA NB, nutrition – 17 LGA NB, p = 0.038). In contrast, in 2012, the use of oral antidiabetic drugs showed a similar result (metformin – three LGA NB, remaining therapies, including nutritional therapy, six LGA NB, p = 0.046). It should be mentioned that the number of patients in some therapeutic groups was very small.

When considering the patients who underwent urgent delivery, six LGA NB, remaining therapies, including nutritional therapy, six LGA NB, p = 0.046). It should be mentioned that the number of patients in some therapeutic groups was very small.

DISCUSSION

The Portuguese population has become increasingly more sedentary and overweight or even obese, due to progressive lifestyle changes. In addition, the increasing migratory flow of people from South America and Asia to Portugal corresponded to higher population diversity. In present times, the financial constraints as well as work demands have resulted in maternity projects taking second place, often delayed by most women. As a result, pregnant mothers are currently older, with higher preconception BMI and risk of pregnancy complications. In our group of pregnant mothers, we found that maternal characteristics were similar in both years.

In fact, the current screening program allowed for an increase in the number of diagnosis. In our study, a 22.8% increase in GDM prevalence (from 4.37% in 2009 to 5.37% in 2012) was found, which if we consider that the area of hospital referral has changed and was subsequently reduced, may reflect a relevant increase.

Different authors assessed GDM prevalence and obtained similar results. Nwose et al. defined the impact of the use of a 75 g OGTT in GDM diagnosis with the "..."
reassessment of clinical records of pregnant mothers who underwent this test between 1999 and 2008. An annual 10.8% additional diagnosis rate was obtained, corresponding to a 46% increase in prevalence. Farah et al. found that this screening was associated to a 10.1% increase in diagnosis rate, from 10.1% to 13.2%, when compared to the previous screening. Ikenoeu et al. compared the perinatal outcomes in pregnant mothers with GDM, using the new criteria vs. pregnant mothers with normal glucose tolerance and found a lower glucose intolerance value in the sub-group of pregnant mothers with only one abnormal screening result, although these pregnant mothers may be at risk of having to start insulin therapy in the presence of a family history of diabetes mellitus. Wery et al. also showed an increase in GDM prevalence to 14% when a 75 g OGTT universal screening was carried out between the 24th and 28th week of pregnancy in 200 consecutive pregnant mothers. An increase in preconception BMI, higher rate of DM2 family history and of DM in previous pregnancies, as well as higher NB’s weight at birth were found, when compared to pregnant mothers without GDM.

One of the major failures in the current screening program is the absence of diagnosis in the third trimester. As described above, the period between the 24th and the 32nd week of pregnancy was used in HAPO to implement this screening. In our Department, the fasting blood glucose level or eventually a new 75 g OGTT in the third trimester is carried out in pregnant mothers with major risk factors – high preconception BMI, excessive weight increase during pregnancy, foetus with estimated weight above the 90th percentile (mainly related to the abdominal circumference) or the presence of hydramnios in a routine third trimester ultrasound imaging. Although not recommended, the authors found that a small percentage of pregnant mothers are diagnosed at that time. In fact, when we analysed the NB’s weight at birth, the average (3,317.3 g) being similar to the average NB’s weight in 2009 (3,331.9 g).

An earlier diagnosis in pregnant mothers with a small metabolic dysfunction allows for a faster response, in order to prevent GDM-related complications. At first, women’s awareness regarding this pathology and the implementation of an adequate nutritional therapy are crucial. Without an adequate metabolic control, which is usually obtained in 1-2 weeks, the option of pharmacological therapy is available. Short-acting and rapid-acting insulin regimens, oral antihyperglycaemic drugs – metformin – or an association of both therapies are currently in use in our Maternity Hospital. In any case, nutritional therapy is always considered for an adequate metabolic control.

Insulin therapy has been preferred in the pharmacological approach associated to the nutritional therapy, with the predominance of a basal regimen with human NPH insulin. Other strategies may be used such as a basal-bolus regimen (human NPH insulin associated to rapid-acting analogue insulin); rapid-acting analogue insulin was used in isolation in a small number of patients. Metformin was used alone or in association to insulin, although its use in pregnancy is not consensual, despite its safety record in several studies. The use of metformin was restricted to patients with clinical characteristics associated to insulin resistance, such as the presence of preconception BMI above 30 Kg/m², polycystic ovarian syndrome, acanthosis nigricans, a higher weight increase or a family history of diabetes mellitus.

A significant reduction in weight increase during pregnancy, as well as a higher use of pharmacological therapy (statistically significant), with a significant reduction in the NB’s weight at birth was found in our group of patients. We therefore consider that we met one of the aims of this screening program. Nevertheless, the average level of Hba1c in the third trimester did not show any variation between the two years, which is in line with what is largely accepted today (this parameter is of little value in most pregnant mothers due to the erythrocyte turnover leading to many false negative results). However, it may be useful in some specific cases although the authors globally question if this method would be the best way to assess GDM’s metabolic control.

Another complication associated to GDM relates to caesarean delivery due to suspicious foetal macrosomia. Although this indication varies according to the institution’s criteria, we used a weight estimate above 4,000 g at our Hospital. In fact, in our study, we found a tendency towards a reduction in the caesarean rate. Elective caesarean sections due to estimated NB’s weight above 4,000 g or dystocia-related urgent caesarean sections were reduced and NRFS-related urgent caesarean increased. These foetuses would probably have a lower oxygen reserve leading to a lower tolerance to the uterine contractility during labour.

Table 6 – Postnatal reclassification in 2009 and in 2012

<table>
<thead>
<tr>
<th></th>
<th>2009 (n = 178 / 79.8%)</th>
<th>2012 (n = 192 / 81%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>153 (86%)</td>
<td>181 (94.3%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Impaired fasting glucose</td>
<td>10 (5.6%)</td>
<td>1 (0.5%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td>12 (6.7%)</td>
<td>9 (4.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Type-2 diabetes mellitus</td>
<td>3 (1.7%)</td>
<td>1 (0.5%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS – not significant
and to an increase in suspicious or even pathologic cardiotocography and therefore to a higher rate of caesarean sections during labour.

In our group of patients, the current screening demonstrated a lower average NB’s weight at birth. In fact, a reduction in LGA NB while a tendency towards an increase in SGA NB was found. The earlier diagnosis and more ‘intensive’ monitoring and treatment may provide an explanation for this tendency. In addition, this fact will contribute for the increase in NRFS-related urgent caesarean rate.

A reclassification test is recommended upon pregnancy and considered crucial for the mother’s future. Although most women present with a normal test, the small percentage with changes allows for a lifestyle modification – appropriate diet and encouraging some physical activity – as well as for referral to Primary Healthcare.

The Portuguese Health Authority (DGS) found a 68% global percentage of women that underwent the postnatal reclassification test in 2011. In our group of patients, this percentage was above that of the general population. Current screening was associated to an increase in normal results for this test, as well as to a reduction in IFG, probably explained by tighter diagnosis criteria.

CONCLUSION

GDM is an increasingly more frequent complication with a maternal and foetal impact not only during pregnancy but also for the mother and newborn’s future.

The authors found that the current screening corresponded to a higher rate of diagnosed GDM, despite a reduction in hospital’s referral area. An increase in the use of pharmacologic therapy was found, aimed at obtaining an adequate metabolic control. We also obtained a reduction in NB’s weight at birth, a reduction in LGA NB’s rate, a tendency to an increase in SGA NB and a reduction in caesarean rate. As regards postnatal reclassification test, an increase in normal tests and a reduction in IFG changes were found.

Additional studies are needed to assess obstetric and perinatal outcomes using the current diagnosis criteria for GDM and a possible increase in SGA NB rate.

OBSERVATIONS

Part of this manuscript was presented at the 3º Congresso Nacional de Obstetricia e Medicina Materno-Fetal, 21-23 November 2013, Porto.

CONFLICTS OF INTEREST

The authors declare that there was no conflict of interests in writing this manuscript.

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REFERENCES

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