GESTATIONAL DIABETES AND ITS NEW CRITERIA OF DIAGNOSIS

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Fetal macrosomia is the most important fetal growth disorder of associated with maternal diabetes, that complicates 15–45% of diabetic pregnancies (pre-gestational or gestational diabetes), being five or six times more frequent than in non-diabetic pregnancies. Its rate correlates with the level of maternal glycemia in the last two quarters of pregnancy. A precarious glycemic control between the 27th and the 32nd week of pregnancy (period of accelerated fetal growth) leads to an increased fetal macrosomia prevalence. However, in spite the intensified treatment, with glycemic values close to normoglycemia, the incidence of macrosomia stays high, considering that at an average glycemia during the day of 104–115mg/dl (5.8–6.4 mmol/l), the macrosomia rate is of 20–30%, which suggests that the limit value of maternal glycemia associated with the emergence of the fetal macrosomia, in pregnancy with diabetes mellitus complications, is much closer to normal than in case of other fetal complications.

According to the current definition[1, 2], the gestational diabetes includes a subgroup of patients with a more severe hyperglycemia which presumes special aspects of management during pregnancy and after birth.

The HAPO Study has been conceived in order to clarify the risks of unfavourable outcomes associated to the stages of mother's intolerance to glucose less severe than those present in the case of diabetes mellitus active during pregnancy [24].

The results of this study[25, 26] have been fully taken into consideration when the recommendations for the diagnosis of gestational diabetes presented in this report have been established.

Key words: gestational diabetes, maternal obesity, hyperglycemia in pregnancy.

Worlwide, diabetes is associated with 10% of the pregnancies, in Romania, only under 5%. We are talking about gestational diabetes in most of the cases, and in only 0.1–0.3% of pregnancies about pregestational diabetes (mainly Type 1 diabetes and rarely Type 2 diabetes or Mody). If before discovering insulin the pregnancy for women with diabetes was very rarely, only 5% reaching full term, the maternal mortality exceeding 25–30% and the perinatal mortality 50–60%, introducing the insulin in the treatment of diabetes has favourably changed the situation, both by increasing the fertility in the case of women with diabetes and by improving the maternal-fetal prognostic. In many countries, the maternal mortality is comparable with that of the non-diabetic pregnant women and the perinatal mortality decreased from 40% in 1940s, to 5–8% in 1970s and to less than 3% (1,2–2%) at the present. Unfortunately, in our country the results are not so good, the perinatal mortality being of 15%, and the fetal congenital malformations emerge in almost 25% of the cases. These are due to metabolism disorders recorded in the first quarter of pregnancy when the organogenesis takes place. Their relation with glycosylated hemoglobin is well established at the present, the excess of some metabolic agents having an important teratogenic potential.

The careful planning and surveillance of the pregnancy by a multidisciplinary team (diabetologist, obstetrician, neonatologist) make posible the early prevention and recognition of maternal-fetal complications[59]. Family planning is crucial for a young woman with diabetes which wishes to have a child.

Pregnant women with diabetes mellitus are divided in two categories:

1. with diabetes which existed prior to pregnancy
2. with diabetes which started during pregnancy.

In both cases, an inadequate treatment significantly increases the maternal risk, the perinatal mortality and morbidity. In spite of the current care, constantly improving, for pregnant women with diabetes mellitus there are still serious issues to be solved:

1. an increase of the congenital anomalies and of the spontaneous miscarriage;
2. an agravation of the prior existing chronic complications;
3. the existance of brittle patients which see a diabetologist later during their pregnancy.

The spontaneous miscarriage in the case of pregnant women with diabetes was estimated in USA, in 2008, to be of 30–60%, according to the metabolic disequilibrium degree present in the moment of conception. The risk of congenital anomalies is of 6–12%, two to five times higher than in the case of the general population.

The etiology of these increased prevalencies was and still is the main topic of intense researches, knowing the fact that hyperglycemia and other metabolic anomalies are teratogenic. The fetal organogenesis is complete in the 8th week after the last menses (six weeks post-conception), thus a glycemic disequilibrium within this period increases both the maternal and fetal risk[60].

The role of the stress in activating the diseases, in affecting the internal equilibrium of the forces, the "homeostasis" or the "internal milieu", as Claude Bernard named it in the 19th century, is known for over 2.500 years.

During pregnancy, the efects of losing the equilibrium lead to disturbances of fetal growth, reducing or accelerating the speed of growth.

There is a question to be asked: is only the size of the macrosomic fetus which predispose it to trauma, or this accelerating growth will influence the whole subsequent evolution of the fetus, including the adult life?

The macrosomic fetus in a mother with diabetes is a particular entity which needes a special care due to its metabolic fragility and its adjusting to the agents in the external environment.

The concept of macrosomia involves a growth process governed by genetic rules and agents of intrauterine environment[62].

In predicting macrosomia becomes important not only the size, but also the speed of reaching that size. Barker theory, of fetal nutrition and of subsequent risks in the life of the adult, is fascinating.

The determinism in the adult's pathology proved to be also valid in the case of macrosomia.

The Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) was published in 2005, this being the first random study regarding gestational diabetes and its risks for pregnancy and offers the necessary evidence for introducing the screening for discovering the gestational diabetes.

The macrosomial fetus in mothers with diabetes has been associated with a giant with clay legs, due to discrepancies between the size and the metabolic fragility.

Macrosomia is the most important disorder of fetal growth, with high risk for both mother and fetus' health. Defining macrosomia is still controversial.

The most common definition is "fetus overweight"[63].Through years there have been elaborated more curves of growth called "curves of intrauterine growth" through which the notion of normal weight at birth it's being established. In 1920, Streeter brings off the first curve of growth starting from the autopsy of dead neonates. This curve was controversial because the intrauterine death of the fetus, as well as its conservation in formalin lead to the modification of the fetal growth. In 1963, Lubchenco and Battaglia bring off a curve of growth which takes into account the gestational age (calculate from the first day of the last menses), the average weight of the fetus, the circumference of the cranium and the waist, through the statistical analysis of the data which followed up the intrauterine growth between the 26th and the 42nd week of pregnancy on 5.635 babies born in Denver, Colorado between 1984 and 1961. Starting then, the notion of percentiles came up: 10, 25, 50, 75, 90. The curve established the "normal" between two standard deviations from the average, or between the 10th and the 90th percentile for a given gestational age. The baby was considered hypertrophic if the weight had been lower or equal to the 10th percentile, and macrosomic if the weight had exceeded the 90th percentile.

The notion of percentile allows the recognition of the abnormal character of some parameters which are situated above or below some prior established norms.

The disadvantage would be that it has eliminated babies which weight could have been apparently increased by some pathological states specific to pregnancy (diabetes, anasarca through

isoimmunization), while those susceptible for decreasing the fetal weight have been incorporated. Because it has been observed that the weight of neonates varies according to the socio economic level, altitude, race, many authors tried to establish curves of growth specific to certain geographical areas.

It is considered that a neonate is overweight (macrosomic) if his weight exceeds by two standard deviations (+ / – 2SD) the average for the gestational age[64].

Nowadays, regardless of the standards used, fetal macrosomia is defined as "a weight at birth higher than the 90th percentile or + / – 2SD from the normal average for the gestational age, gender and race".

In case of full term pregnancy, the weight must be higher than 4.000 g, at 34 weeks higher than 3.400 g, and at 30 weeks higher than 2.000 g.

There are two types of macrosomia:

– proportionate (symmetric) – balanced fetal growth, with normal weight coefficient, which has a preponderant genetic cause,

– disproportionate (asymmetric) – excesively developed adipose tissue and selective splanchnomegaly, including cardiomegaly, but with normal brain and kidneys, increased weight coefficient, more frequently seen in pregnancies with gestational and pre-gestational diabetes complications.

The influence of intrauterine fetal nutrition and of subsequent risks in the adult life is fascinating. The determinism in the adult pathology proved to be valid also in the case of macrosomia.

MATERNAL DIABETES

Fetal macrosomia is the most important disorder of fetal growth associated with maternal diabetes, which complicates 15–45% from pregnancies with diabetes (diabetes mellitus pre-gestational or gestational), being five or six times more frequent than in non-diabetic pregnancies. Its rate correlates with the level of maternal glycemia in the last two quarters of pregnancy. A precarious glycemic control between the 27th and the 32nd week of pregnancy (period of accelerated fetal growth) accompanies the growth of fetal macrosomia prevalence. However, in spite the intensified treatment, with glycemic values close to normoglycemia, the incidence of macrosomia stays high, considering that at an average glycemia during the day of 104–115 mg/dl (5.8–6.4 mmol/l), the macrosomia rate is of 20–30%, which suggests that the limit value of maternal glycemia associated with the emergence of the fetal macrosomia, in pregnancy with diabetes mellitus complications, is much closer to normal than in case of other fetal complications. As a result, the glycemic targets for preventing the fetal macrosomia on pregnant women with diabetes, should be:

– pre-diabetes (glycemia *à jeun*) 63–123 mg/dl (3.5–7 mmol/l)

– preprandrial glycemia 60–105 mg/dl (3.5–5.8 mmol/l)

– postprandial glycemia 60–120 mg/dl (3.3–6.7 mmol/l)

These values are comparable to those seen in non-diabetes pregnancy, which are situated between 52–115 mg/dl (2.9–6.4 mmol/l), with an average of 85 mg/dl (4.7 mmol/l). Kitzmiller and collaborators considers that the glycemic threshold value for the emergence of fetal macrosomia is a postprandial apex higher than 130 mg/dl (7.2 mmol/l), showing that an average postprandial glycemia under 110mg/dl (6.1 mmol/l) can also be associated with a delay in fetal growth and babies small for the gestational age. Mello and collaborators showed, after analyzing 98 pregnancies on women with Type 1 diabetes between 1990–1997, that only a daily average value of glycemia lower or equal to 85 mg/dl (5.3 mmol/l), reached early in the second quarter and continued in the third quarter associates with a normal fetal size at birth. The incidence of fetal macrosomia in this group was of 5.4% comparing to 37.8% on women with a glycemia higher than 95 mg/dl (approximately 100 mg/dl) in the second quarter of pregnancy and lower than 95 mg/dl in the third quarter and of 54.2% on women with glycemia higher than 95 mg/dl in the last two quarters of pregnancy (but with an average glycemia of 105–106 mg/dl). This level was similar to the level seen in non-diabetic pregnancies (8.5% in the control group) and the lower glycemic values didn't correlate with the increase of the incidence of delay in fetal growth or severe hypoglycemia.

Besides glycemic control and independent of this, fetal macrosomia risk correlates also with the maternal weight prior to pregnancy, as well as with the maternal ponderal gain during pregnancy.

In the pathogenesis of fetal macrosomia, the maternal hyperglycemia has got the main role and leads to fetal hyperglycemia, followed by the stimulating of the pancreatic beta cells, with the

increase of fetal insulin synthesis. The role of maternal hyperglycemia in the emergence of fetal macrosomia is supported also by the ascertainment that, by intensifying the insulin treatment, with normalizing the glycemic values, the size of the baby tends to normal, as well as its aspect at birth. This improvement is partially due to the decrease of adipose tissue which accumulates in the last 8–10 weeks of pregnancy. Besides glucose, the fetal insulin secretion is stimulated also by the branched amino acids, free fatty acids and tryglicerides. An abnormal function of pancreatic beta cells may emerge in the first quarter of pregnancy, the appearance of high levels of insulin in the amniotic fluid between the 14th and the 20th week of pregnancy pleading in this respect. Fetal hyperinsulinemia is accompanied also by the increased transfer of nutrients between mother and fetus, followed by the stimulating of lipogenesis and fetal anabolism, with the increase of adipose tissue quantity and splanchnomegaly. The increase of the mass of adipose tissue, as a result of triglycerides accumulation, takes place by increasing the number and the volume of adipose cells, as well as by increasing the quantity of glycogen in the adipose tissue. Increased fetal anabolism is followed by cellular hyperplasia and hypertrophy, with increasing the internal organs of the fetus (heart, liver, spleen, pancreatic tissue, adipose tissue, adrenal glands), except the brain which remains normal. The tendency of diabetic mothers' babies of being heavier and longer than the average for the gestational age and sex, becomes clinical evident after the 28th week of pregnancy. Another explanation of accelerating the fetal growth in the second quarter of pregnancy would be the exceeding binding of the fetal insulin or proinsulin to somatomedin receptors, with the inducing of a promotor effect of growth.

Fetal hyperinsulinemia is also involved in the delay of fetal lung maturity by the inadequate production of surfactant, the same as in the delay of passing from the fetal hemoglobin synthesis to the adult one.

The fetal reserves of oxygen may be even more altered by the placentary lesions and, in case of precarious maternal metabolic control, of increasing HbA1c proportion.

As a response to the acute/chronic episodes of fetal hypoxia, emerges the emphasis of extramedullary erythropoiesis and polycythemia. The episodes of fetal hypoxia may be responsible of the sudden death of the macrosomic fetus.

Fetal macrosomia is frequently associated with an increase of placentary mass, through proliferation in excess of cyto- and syncytiotrophoblast. Mature villi, as well as villi with syncytial nodes emerges more frequently in diabetes, suggesting an increase stronger than normally. It cannot be said if the excessive increase of the placenta can compensate the volume decrease of intervillous spaces emerged through excessive ramification of chorionic villi. The decrease of intervillous space may reduce the fetus tolerance to a sudden decrease of the sanguine perfusion at this level.

The ultrasonographic observation reveals, after the 24th week of pregnancy an over normal increase of the fetal abdominal circumference (1.36 cm per week, comparing with 0.901cm per week in case of non-diabetic pregnancies), associated with a normal increase of the head, even in the presence of maternal hypeglicemia. The strong increase of the abdominal circumference is due to preferential depostis of fat in the abdominal and interscapular regions. The central deposit of fat is one of the diabetic macrosomia characteristics.

Macrosomic neonates are very much alike, being fleshly, plethoric, with cushingoid facies, glassy skin, red-blue, with petechial rush and periumbilical hemorrhage. The neonatal icterus is more pronounced and lasts longer. At the level of conjunctive membrane can be seen in venous ectasia with pervascular edema. There are also more frequent the congenital malformations (cardiovascular, of central nervous system, skull, extremites etc). The polyhydraminos is frequently seen as a result of increased osmolarity of amniotic fluid (due to the excess of glucose), of fetal polyuria (consequence of fetal hyperglycemia) and of fetal deglutition decrease. The fetal macrosomia increases the frequency of traumas at natural birth. The risk of brachial plexus injury through shoulder dystocia is of approximately 7% for babies with weight higher than 4.000 grams, even up to 14% for macrosomic neonates from diabetic mothers, due to the fact that the latters have a higher degree of abdominal obesity.In the same time, the neonates may present states of shock or metabolic acidosis and / or respiratory, having a very complicated neonatal evolution. The most frequent neonatal complications are: neonatal hypoglycemia, polycythemia, hyperbilirubinemia, coagulation disorders.

MATERNAL OBESITY

The secretive effort of pancreatic beta cells is huge in case of obese pregnant women, case in which even in non-gestational period the periferic insulin resistance exists.

At the same time, the incidence of gestational diabetes in case of obese women is considerably higher, up to 10–15%. The effects of maternal obesity on the fetus are due to the increased transfer of free fatty acids and glucose from mother to fetus, with the emergence of macrosomia.

RECOMANDATIONS OF INTERNATIONAL ASSOCIATION OF DIABETES AND PREGNANCY STUDY GROUPS REGARDING THE DIAGNOSIS AND CLASIFICATION OF HYPERGLYCEMIA IN PREGNANCY

In 1988, there were formed the International Association of Diabetes and Pregnancy Study Groups (IADPSG), as an umbrella organization meant to facilitate the cooperation between distinct regional and national groups, which main or significant target is diabetes and pregnancy.

On 11th-12th June 2008, IADPSG sponsored the International Conference-Workshop regarding the diagnosis and clasification of diabetes mellitus and gestational which took place in Pasadena, California. Over 225 participants from 40 countries reviewed the published outcomes of HAPO Study (Hyperglycemia and Adverse Pregnancy Outcome), as well as the outcomes of other activities which investigated the association between the level of mother's glycemia and the long term outcomes in case of the baby.

The gestational diabetes, a frequent complication in pregnancy, is defined as "any level of intolerance to glucose which starts or is recognized for the first time during pregnancy"[1, 2]. The initial criteria for its diagnosis have been established over forty years ago[3] and, with amendments, they are used nowadays. This criteria have been chosen in order to identify the women with a high risk of developing diabetes mellitus after pregnancy[5] or have been derived from the criteria used for women with no pregnancy[6] and don't necessarily identify the pregnancies with high risk of unfavourable outcome. By consensus, the diabetes mellitus active during pregnancy, symptomatic or asymtomatic, is associated with high risk on fetus.

Some voices adjudged the risks of the unfavourable outcomes associate to gestational diabetes, such as the weight high for gestational age (LGA – large for gestational age), the excess of fetal adiposity and the higher rate of cesarean sections, to the characteristics which generate confusions, such as obesity, an older mother or other medical complications, and not to the intolerance to glucose[7–9].

The tendency of the medical staff to expect unfavourable outcomes may increase the morbidity due to the high degree of intervention[10].

Other voices suggest that the criteria used at present for gestational diabetes' diagnosis are too restrictive and that lower levels of hyperglycemia increase the risk of unfavourable perinatal outcomes.

Recently, a study of cost efficiency performed by the National Institute for Health and Clinical Excellence form Great Britain concluded that "screening, diagnosis and the treatment of gestational diabetes are cost efficient".

According to the current definition[1, 2], the gestational diabetes includes a subgroup of patients with a more severe hyperglycemia which presumes special aspects of management during pregnancy and after birth.

The HAPO Study has been conceived in order to clarify the risks of unfavourable outcomes associated to the stages of mother's intolerance to glucose less severe than those present in the case of diabetes mellitus active during pregnancy[24].

The results of this study[25, 26] have been fully taken into consideration when the recommendations for the diagnosis of gestational diabetes presented in this report have been established.

The target of HAPO Study was to clarify the associations between mother's levels of glycemia lower than those used for the diagnosis of diabetes mellitus and the birth's outcome[24, 25]. This has been effectuated through a test of tolerance to glucose with 75 grams of glucose orally administrated (TTGO) to a heterogeneous cohort, diverse from the point of view of culture, nationality, ethnie, formed from approximately 25.000 women in the third quarter of pregnancy.

The main targets in the cohort with blind design from HAPO were the weight at birth > percentile 90, birth through primary cesarean section, neonatal hypoglycemia clinically defined and the level of peptide C in the umbilical cord > percentile 90. The secondary targets were the pre-eclampsia, the premature birth, shoulder dystocia / lesions at birth, hyperbilirubinemia and neonatal intensive therapy.

THE THRESHOLD VALUES FOR THE DIAGNOSIS OF GESTATIONAL DIABETES OR DIABETES MELLITUS MANIFEST IN PREGNANCY

For gestational diabetes diagnostic

Value of glycemia value (%)	Threshold value of glycemia		Over threshold
	mmol/l	mg/dl	cumulated
FPC	5.1	92	8.3
Glycemia 1h	10	180	14.0
Gliycemia 2h	8.5	153	16.1

One or more values obtained as a result of a test of tolerance to glucose with 75 g must be reached in order to establish the diagnosis of gestational diabetes.

In order to diagnose diabetes mellitus manifest in pregnancy

Glycemic parameter consensus	Threshold value reched by
FPC (126 mg/dl	Higher or equal to 7.9 mmol/l
AIC	Higher or equal to 6.5% (standardized in DCCT/UKPDS)
Aleatory value of glycemia	Higher or equal to 11.1 mmol/l (300 mg/dl)

One of these must be fulfilled in order to identify the patient with diabetes mellitus manifest in pregnancy. In case an aleatory value of glycemia is the initial parameter, the attempt of diagnose diabetes mellitus in pregnancy must be confirmed by FPG or A1C, using a standardized analysis in DCCT/UKPDS.

The staged analysis of the data in the HAPO Study lead to the recommendation of FPG values of glycemia at 1 h and 2 h, indicated above as threshold values of diagnosis. These threshold values are the average values of glycemia at which the probabilities of weight at birth > percentile 90, the levels of peptide C in the umbilical cord > percentile 90 and the percentage of adiposity > percentile 90 reached 1.75 times the estimated probability of these objectives on average values of glycemia on the assumption of logistic regression models fully adjusted. At least one of these threshold values must be reached or exceeded in order to establish the diagnosis of gestational diabetes. The measuring just of FPG identified an proportion of 8.3% from the cohort with gestational diabetes. Adding the measuring of glycemia at 1 h identified an additional proportion of 5.7%. Adding the measuring of glycemia at 2 h identified another proportion of 2.1% from the cohort.

THE TRACKING AND THE DIAGNOSIS OF DIABETES MELLITUS MANIFEST IN PREGNANCY

The international conferences over gestational diabetes defined this affection as "any level of intolerance to glucose which starts or is recognized for the first time during pregnancy"[1, 2]. The definition has been applied whether they appeal or not to insulin therapy or if the hyperglycemia still persists after pregnancy.

The possibility that the intolerance could be prior to birth has not been excluded.

This facilitates a uniform strategy for tracking and classification of gestational diabetes, but there are some constraints.

Taking into account that the current epidemic of obesity and diabetes mellitus leads to more cases of Type 2 diabetes among young women, the number of undiagnosed patients prior to pregnancy is increasing [49, 50].

THE STRATEGY FOR DETECTING AND DIAGNOSING THE HYPERGLYCEMIC DISORDERS IN PREGNANCY

It shall be performed on women without an established diagnosis of diabetes mellitus prior to pregnancy. The postpartum measuring of glycemia must be performed on all women diagnosed with diabetes mellitus manifest during pregnancy or gestational diabetes.

The first prenatal visit

It shall be measured the FPC, A1C or an aleatory value of glycemia on all women or just on those with high risk (the decision of performing these sanguine tests in order to determine the glycemia on all pregnant women or just on those with characteristics which indicate high risk of diabetes shall be taken on the basis of the fund frequency of glucose metabolism anomalies in the respective population and of the local circumstances.

In the case in which the outcomes indicate diabetes mellitus manifest according to prior criteria, treatment and observation as in the case of diabetes mellitus pre-existent.

In the case in which the outcomes are not diagnostic for the diabetes mellitus manifest and

for glycemia *à jeun* higher or equal to 5.1 mmol/l (92 mg/dl), dar lower than 7.0 mmol/l (126 mg/dl), it shall be diagnosed the gestational diabetes.

Also the glycemia *à jeun* higher than 5.1 mmol/l (92 mg/dl) shall be investigated for gestational diabetes between 24 and 28 weeks of pregnancy with TTGO wu 75 g of glucose. The studies committee concluded that there haven't been performed enough studies to know if the generalized testing for the diagnostic and treatment of gestational diabetes associates with benefits before the interval in which these tests are performed, between 24 and 28 weeks of pregnancy.

24 AND 28 WEEKS OF PREGNANCY: THE DIAGNOSIS OF GESTATIONAL DIABETES

TTGO with 75 g at 2h: shall be performed after alimentary repose during the night on all women on which it hadn't been tracked diabetes mellitus manifest or gestational diabetes during the tests performed earlier in the evolution of the current pregnancy.

Diabetes mellitus manifest in the case in which glycemia *à jeun* is higher or equal to 7.0 mmol/l (126 mg/dl).

Gestational diabetes in the case in which one or more values are equal or higher than the threshold values earlier indicated.

Normal in the case in which the values identified in TTGO are lower than the threshold values prior indicated.

The problem bound to the classification of women at which the probability of diabetes mellitus existing prior to pregnancy (diabetes mellitus manifest) to be noticed for the first time during pregnancy had been approached through presentations performed by experienced clinicians / researchers, accompanied by interactive discussions.

Some arguments have been brought in favor of identification of women with diabetes mellitus manifest, as a distinct group of women:

– high risk of congenital anomalies on babies[51];
– the risk of complication of diabetes mellitus (nephropathy and retinopathy) which requires treatment during pregnancy;
– the necessity of immediate therapeutic intervention and careful observation during pregnancy, in order to assure quick rehabilitation of normal levels of glycemia[53, 54];
– the necessity of assuring the confirmation and adequate treatment of diabetes mellitus after pregnancy.

IDENTIFICATION OF DIABETES MELLITUS MANIFEST

The moment and the way in which women with diabetes mellitus manifest during pregnancy (which haven't been prior diagnosed) can be identified and the way in which diabetes mellitus manifest is defined have been taken into consideration during the meeting of International Association of Diabetes and Pregnancy Study Groups (IADPSG) in Pasadena and subsequent.

There has been existed the consensus that this assessment must be performed during the first visit of pre-natal assistance.

Members of the consensus committee of IADPSG declared themselves in favor of using any available glycemic parameter of a certified laboratory (FPG, the aleatory value of glycemia or A1C) for initial tracking of potential cases.

A committee of experts have recently recommended a value of A1c higher or equal to 6.5% (measured in a standardized laboratory / aligned with the tests in DCCT – Diabetes Control and Complications Trial / UKPDS – UK Prospective Diabetes Study) to be used to diagnose diabetes mellitus in absence of pregnancy[55], but the recommendation of using exclusively one single test is not feasible.

The cost and standardization of A1C testing are aspects which must be taken into consideration and the hemoglobinic versions are prevalent on some populational groups.

An attempt to diagnose the diabetes mellitus manifest on the basis of aleatory value of glycemia must be confirmed either with a value of FPG or A1C higher or equal to the threshold value, using a method standardized / aligned with DCCT / UKPDS[56].