

PROBING GLYCEMIC VARIABILITY WITH ORAL GLUCOSE TOLERANCE TESTING

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Abstract

The Oral Glucose Tolerance Test (OGTT) has traditionally served as a valuable diagnostic tool for conditions such as diabetes mellitus, gestational diabetes, glucose intolerance, reactional hypoglycemia, and diabetes associated with cystic fibrosis. However, over the past decade, its application has been predominantly restricted to fasting blood glucose measurements and glycated hemoglobin levels, sparking controversial debates. Recent studies, in contrast, reaffirm the significance of OGTT as a reference diagnostic tool for assessing glycemic variations, identifying a decrease in glucose tolerance (a marker for cardiovascular complications and type 2 diabetes), and diagnosing gestational diabetes. Moreover, OGTT has been proposed as a quantitative method to assess insulin secretion and insulin sensitivity, offering the advantage of dynamic measurements under stimulation conditions, which sets it apart from tests like fasting blood glucose measurements.

This study aims to analyze the OGTT profiles of patients referred to the Institut Pasteur of Côte d'Ivoire (IPCI) between 2013 and 2016. By examining OGTT results in this cohort, we seek to contribute to the management and prevention of diabetes and its associated cardiovascular risks.

Introduction

The Oral Test of Tolerance of Glucose (OGTT) was mainly widespread to diagnose the diabetes mellitus, gestational diabetes, glucose intolerance, reactional hypoglycemia [1] and also dependent diabetes has the cystic fibrose [2]. However, in the last decade, the use of this dynamic test was limited to the simple measurement of the glycemia in empty stomach and glycated haemoglobin, where the idea of abandoned raised many polemic [3]. Nevertheless, all the recent studies mainly quoted OGTT like an able diagnosis of reference to evaluate glycemia variations and to show a diminution of the tolerance to glucose (marker of cardiovascular complications and

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diabetes of the type 2), or of gestational diabetes [3]. This test was also proposed, quantitatively to estimate the insulin secretion and the sensitivity of insulin. It has advantage of measuring these parameters under dynamic conditions of the stimulation [4], which is not the case for other tests like "glycemia measure in empty stomach" [5, 6]. In order to perform control of mellitus diabetes and also to prevent risks of cardiovascular diseases, we will focus our study on the analysis of profile OGTT of referred patients from 2013 to 2016 to Institute Pasteur of Côte d'Ivoire (IPCI).

Material and Methods

Framework and population of study

The study was carried out in Pasteur Institute of Côte d'Ivoire (IPCI), Cocody / Abidjan site. We conducted a cross-sectional and retrospective study from 2013 to 2016. Our study population of 100 subjects consisted mainly of pregnant women aged between 18 and 49 years; some of them were interned in the Hospital University of Cocody.

1.3. Material of study

Material used for this study was constituted of supports of data-gathering (Registers of consultation), computers (numerical data) for the recording and the analysis of the data and a printer for the impression of the cards results OGTT. A statistical software of analysis for the treatment of data, rulers, pens to mark the already treated cards. On each register were mentioned the number of the register and the period concerning.

Methods

Criterion of inclusion

In this study, the pregnant women whose age was equal to or higher than 18 years and less than or equal to 49 years were included.

Criterion of exclusion

The pregnant women whose age was lower than 17 years and higher than 49 years and who had a curve which did not present a peak hyperglycemic were excluded.

Data collected

The collection of the data was carried out by consulting clinical files and numerical data in Department of Clinical and Fundamental Biochemistry of Pasteur Institute „IPCI“ of Côte d'Ivoire between 2013 and 2016. Clinical parameters was transferred on a card called "slip patient" including: identification of patient, results of glycemia and normal values, the profile OGTT of the subject by a curve of variation of glycemia according to time, the parameters of hyperglycemia: hyperglycemia Arrow or hyperglycemia pointer (HP), time of return to the initial glycemia "TRGLyi"; and last part indicating appreciation, comment and the signature of biologist.

In connection with the studied parameters of hyperglycemia, it should be noted that: The Hyperglycemia arrow „HP or ΔG “, was the difference between the maximum value and the minimal value of glycemia. It is normal if it lies between 0.20 and 0.5 g/l. The time of return to the initial glycemia "TRGLyi" was obtained by carrying out the projection of the glycemia on the axis of times in minutes; it is normal if it lies between 2 and 3 hours. The Return to initial glycemia "RGLyi" indicated the return to the starting glycemia.

Statistical Analysis of Data

Data statistical analysis was carried out using GraphPad Prism software 6.01. The Anova test was used to compare the averages. The difference was significant for P value's: $P < 0.05$.

Results

The mean age of the subjects was 33.29 ± 6.55 years. The youngest was 18 years old. The highest participation was recorded with women aged between 30 and 40 (55%); followed by women aged 20-30 (27%), and over 40

years (17%) (Table I). The majority of subjects had normal fasting glucose (GJ: 97%); fasting glucose abnormality (FGA: 3%) ; intolerance to glucose (ITG: 18%); and postprandial hyperglycemia (PPH: 43%)(Table II).

Table I: Distribution of subjects by age group

Age category(years)	Number of subjects	Percentage (%)
Age < 20	1	1
$20 \leq \text{Age} < 25$	9	9
$25 \leq \text{Age} < 30$	18	18
$30 \leq \text{Age} < 35$	28	28
$35 \leq \text{Age} < 40$	27	27
$40 \leq \text{Age} \leq 49$	17	17

Table II: Rate of pathological glycemia among the subjects

	Normal Value of the laboratory (g/l)	Number of subjects with abnormal blood glucose(%)	Type of anomaly
T₀ in Jeun	0.74 – 1.10 ; (N = 97%)	N = 03	FGA
After two hours	<1.20	N = 18	IGT
		N = 43	PPH

FGA : Fasting Glucose Abnormality ; PPH : PostPrandial Hyperglycemia ;

IGT: Impaired Glucose Tolerance

The majority of subjects (77%) did not return to the initial blood glucose level, compared to 23% whose blood glucose level returned to the initial value (TRglyi).No non-return to initial glycemia status on 77% mentioned was more representative for women aged 30-40 years (60%). The difference is significant compared to age groups between 25 and 30 years (18%) and beyond 40 years (13%). On the other hand, those with a return to the initial blood glucose level of 23% previously indicated were more represented in subjects aged between 40 and 49 years, but the difference was not significant compared to the other age groups (Figure 1). The Figure 2 shows the proportion of subjects with normal return time (60.87%) was twice that of abnormal return time (33.13%).

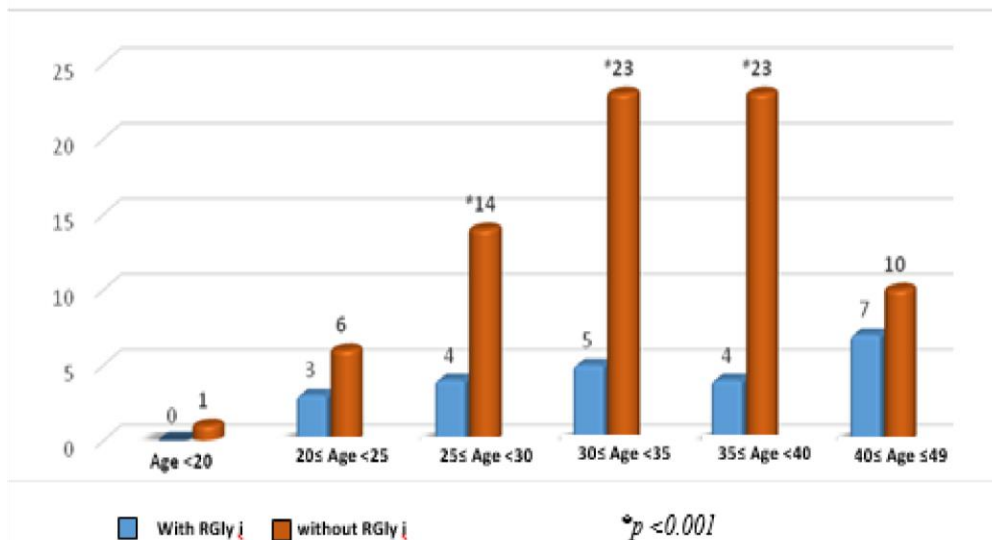
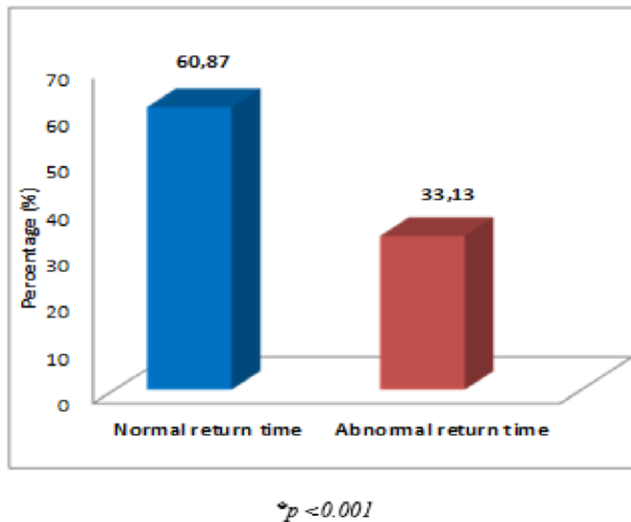
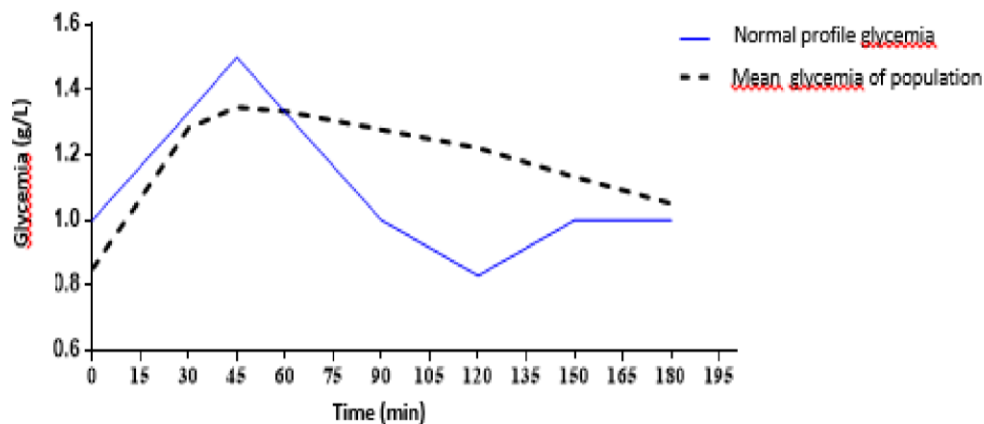


Figure 1: Age distribution of subjects according to the return time or no to initial blood glucose**Figure 2: Distribution of subjects according to the normal or no return time to initial blood glucose**

The mean values of glycemia in population studied were greater than the normal values from the time $T = 60$ min, it means that after 1 h post-charge, with a significant difference between 90 and 150 min (Figure 3). The profile according to the state of return or not to the initial blood glucose is presented in Figure 4. In subjects whose blood glucose did not return to its original value, the profile was found to be above that of normal blood glucose from time $T = 60$ min, that's to say after 1 h post-charge with a significant glycemia. In subjects whose glycemia returned to their original value, showed that the blood glucose level of the subjects concerned was higher than normal value glycemia between 75 and 140 min, and below 140 min with a return time to the initial blood glucose level. Blood glucose in subjects with a return to initial glucose and those with no return, had a similar OGTT profile in the interval (0 min-30 min) with an almost identical initial blood glucose at T_0 . However, for periods longer than 30 min, the blood glucose level of subjects with a return to the initial value remained lower than that of subjects who did not return to the initial glucose level, with a significant difference.

**Figure 3: Overall mean oral glucose tolerance test profile according to the time**

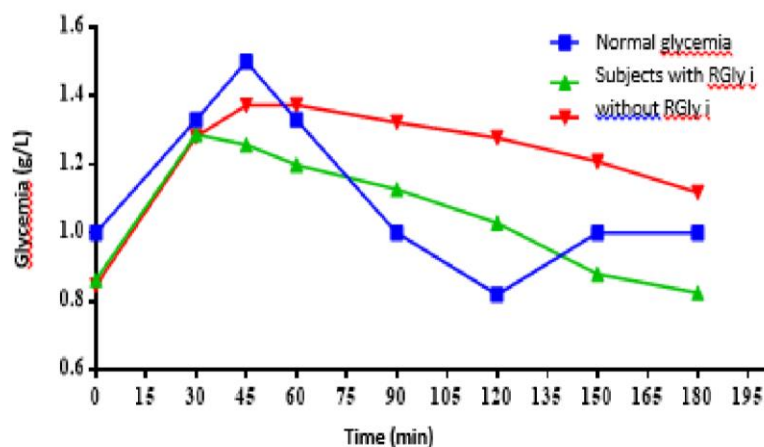


Figure 4: Profile of oral glucose tolerance test according to the statute return or not to the initial blood glucose

We noted also percentage of subjects with an abnormal hyperglycemic pointer (HP): (FH normal = 40%, HP abnormal = 60%) was high. Considering together FH values and return or not to the initial blood glucose (RGlyi), four situations were identified: subjects HP normal with RGlyi 37.5%; subjects HP normal without RGlyi 62.5 %; subjects HP abnormal with RGlyi 13.33 % and subjects HP abnormal without RGlyi 86.67%; Figures 5A and 5B.

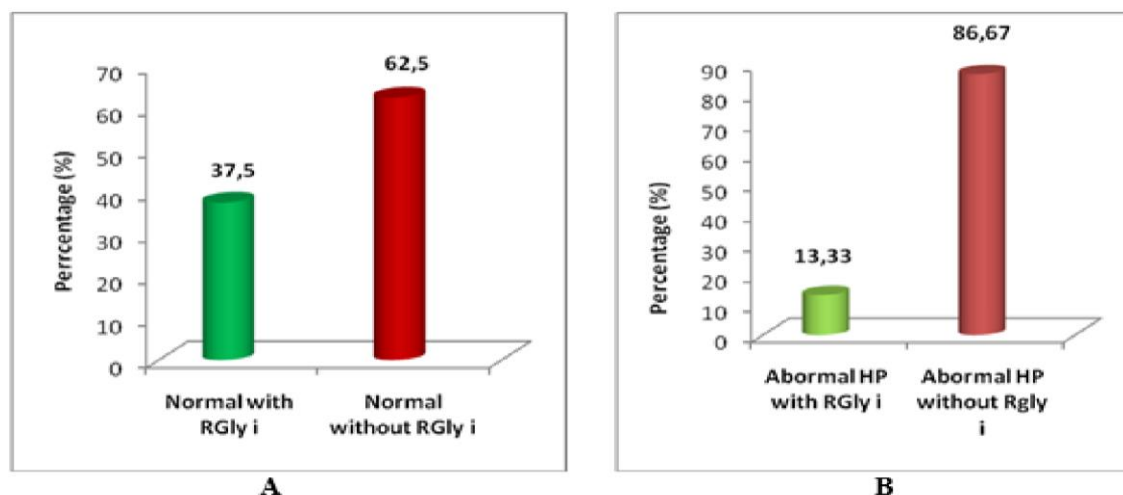


Figure 5: Distribution of the subjects according to the statute normal or abnormal of the pointer of hyperglycemia (HP)

A: Pointer of normal hyperglycemia (HP) normal with or not return to the intialglycemia **B:** Pointer of abnormal hyperglycemia (HP) with or not return to the intialglycemia

Discussion

Population of this study had on average 33.29 years old, so they were adults. This category of subjects was similar to those used by author in 2012, in which average year old was 27.3 used for an OGTT in the regional maternity of Nancy (France)[7]. The majority of the women of the study had not let observe any return to the initial glycemia, with situations of IGT or exposure to the diabetes. This observation was in accordance to the study leaded by Abodo in 2016, with a prevalence of 5.7% of diabetes noted before 2000 and 9.6% into 2010 [8]. It is

the same for the conclusions of the congress " Diabetes and Pregnancy " in Salzburg (Austria) which indicated a prevalence of 4.4% during tests OGTT carried out among pregnant women [7].

The strong proportion of the old women from 30 to 40 years who didn't show a return to the initial glycemia is a kind of confirmation with observations of sernyak and al. [9]. According to the author, the prevalence of the diabetes would strongly increase with the age, going from 8% for subjects less than 40 years to 25% for subjects more than 60 years.

The analysis of the population according to the normal statute or not of the glycemia showed that the majority of the subjects have a normal fasting glucose (NFG) that is to say 97%, a fasting glucose abnormality (FGA: 3%) including moderated hyperglycemia an empty stomach (MHS) with 2%, and diabetes of the type 2 (DT2) with 1%, an impaired glucose Tolerance (IGT) with 28% and an hyperglycemia postprandiale (HPP) with 43%. The HPP (43%) and IGT (18%) raised in this study would indicate a predisposition of the subjects to cardiovascular risks. Indeed, epidemiologic studies showed that the hyperglycemia postprandiale (HPP) is a cardiovascular marker of risk for the subject non diabetic and diabetic type 2 [10, 11]. Moreover, there is a great number of clinical and experimental arguments in favor of functional vascular modifications in postprandial period [12]. This same opinion was shared by authors in a study entitled "Cardiovascular Health Study" [13]. According to this study, a strong predictive value of cardiovascular events exists for the glycemia after oral load of glucose compared to the glycemia in an empty stomach. Indeed, the study on the new criteria of diagnosis and classification of mellitus diabetes carried out by, showed that subjects presenting an IGT or a MHS were exposed to the risk of diabetes and the macroone [14]. According to these authors, two categories (IGT and MHS) are classified like subjects having an abnormal glycoregulation. It is in this same logic that showed the interest of the OGTT by specifying that in the absence of this test, nearly 2/3 of the patients would not have been detected in the case of anomalies of the glucidic metabolism [15]. The profiles of OGTT in this study showed cases of tolerance and intolerance to glucose, with a glycemic peak before one hour post-load of glucose. Impaired glucose tolerance (IGT) could be explained as follows:

In a case of an empty stomach, the great majority of the glucose produced by the liver was used by fabrics not sensitive to the insulin (brain, retina, erythrocytes) as essential energy substrate. Therefore administration by oral way of glucose trained an accrual on the level of fabrics sensitive to insulin [16]. Thus, a defect of use of glucose on the level of the β cells could be caused a reduction of the insulin secretion. Moreover, for lack of insulin, the glycemia of the subject would remain always high and would have as a consequence a no return with the basic glycemia. Thus, the deterioration of the transport of glucose towards cells would be the origin of serious pathologies like the insulindependent diabetes [17]. Indeed, in the insulin-dependent diabetes, auto-immun disease, the destruction of β cells Langerhans involves an insulin deficiency. This one results in a strong hyperglycemia because of the defection of penetration of glucose in the muscular cells and the increasing in the hepatic production of glucose. This type of diabetes implies in a significant way the glucidic and lipidic metabolism. The hyperglycemia is the parameter diagnosis of this pathology. The bad entry of glucose in peripheral fabrics, muscles initially, and from the increasing in the hepatic production of glucose, would result at the same time from the insulin deficiency and resistance of fabrics to the hormone. This situation could lead to an accumulation of triglycerides and a gain of weight [17]. It could thus have an accumulation of triglycerides or storage of glucose in fat fabrics thus with a gain of weight. This fatty fabric excess would be then toxic for the pancreatic cells causing the pancreatitis and would make obstruction with the arteries thus causing the atherosclerosis factor of cardiovascular risks [18]. The constant increasing without relapsing of the glycemia in the intolerant subjects to glucose could be also explained by several hormonal phenomena. Indeed, the absolute or relative deficit of insulin associated to the increasing of hormones of regulation (glucagon, catecholamines,

cortisol and growth hormone) was responsible for a hyperglycemia by the following ways: an acceleration of the degradation of glycogen, a reduction in the tissue use of glucose and an increasing in the production of glucose by another source [19]. This last way would be the principal cause of the hyperglycemia and would be facilitated by the increasing in the precursors (acid amino, lactate and glycerol) in the production of glucose due to the hormones of down regulation. Moreover, hyperglycemia with osmotic diuresis involves, dehydration and reduction in the renal perfusion. That leads to the reduction in the renal excretion of the glucose which is a major mechanism of defense against the hyperglycemia [20]. However, if this anomaly persists, the subject will then be exposed at the risk of renal insufficiency and thus indirectly at the cardiovascular risk [21].

According to this author, beyond the anomalies of albumin in the urinary excretion, which has occurred of a renal insufficiency marks a true turning at the diabetic type 2 in cardiovascular term of forecast. Thus, a deterioration even beginner of the glomerular flow of filtration can be regarded as a predictive factor independent of the mortality and which has occurred of cardiovascular events.

From this study, it is come out that despite the absence of time of return to the basal glycemia of the total population, the hyperglycemia pointer (FP) appeared normal (0.496 g/l). Thus, it states that any profile having a good glycemic value of the delta (difference between the maximum value and the minimal value of the glycemia) would not be inevitably safe from a diabetes. Within the framework of this study, the delta glycemic or (FP) was normal when it layed between 0.20 and 0.5 g/l (usual values of the laboratory of biochemistry of the IPCI). The subjects without return to the initial glycemia whose did not present a peak of hyperglycemia, would let suggest an anomaly of absorption of the glucose, which would be explained by non-absorption of glucose by the patient, nausea, vomiting [22] an early peak glycemic not tested by the first glycemia at one hour, drug or toxic substances interfering with glycolysis (aspirin, acid ascorbic, alcohol, beta-blockers...) [23]. The test could also be disturbed by pathological situations modifying these parameters: digestive drugs, endocrine pathologies, affections with reduction in the motility and intestinal absorption, like certain renal pathologies with renal escape of glucose. Some authors noted that the variations of the glycemia depend on a great number of factors, of which gastric draining, insulin secretion, the secretion of intestinal hormones for purpose " incretine ", the hepatic production of glucose, the peripheral sensitivity to glucose, the preliminary stock of glycogen tributary partly of the nutritional state [24].

On the level of the population, more half (60%) expressed an anomaly on the level of the FH. The results obtained of coupling FH with the phenomenon of RGlyi in figure 5 came to enhance the idea of the high anomaly presented by Figure 5 This figure showed that the majority of the subjects having a normal FH did not tolerate glucose all the same, and that in spite of a statute of abnormal FH, it was still the proportion of subjects which had IGT which dominated with a representation of more than 86.67 %. The FH still called delta glycemic by some authors should not be higher than 0,5g/l (maximum normal value), but should rather lie between 0.20 and 0.50 g/l. The two cases of subject (normal HP and abnormal HP) would present an anomaly at the level of the glucidic metabolism because of the glycemia which did not return to initial at the end of the test. Moreover, the averages on the level of the two groups of subjects (0.53 g/l) and (0.65 g/l) respectively normal HP with RGlyi and normal HP without RGlyi, still come to support occurred of intolerance to the glucose of the last group.

However, the time of the complete metabolisation of glucose until reaching basic glycemia shows us an idea different from the preceding results. Indeed, one noticed in this study that the subjects with abnormal HP presented a time of return to the initial glycemia (TRGlyi) normal and had a percentage doubly higher (60.87%) than that their counterparts which posted abnormal TRGlyi (33.13%). These data suggested that it is not enough for a patient to tolerate well glucose to be safe from certain pathologies of a hormonal nature, even pancreatic related to the excessive sugar consumption. In other words, to have a time of return to the initial glycemia necessarily

does not allow to justify a good metabolism of glucose by the organism receiver, because it is rather ideal for the organism to better metabolize sugar but that must be done in normal time that is between 2 and 3 hours after ingestion [7]. It implies that the return should not be made in an abrupt way, fast or late (case of insulinopenia); but rather in a progressive way so that the organism can optimize the glucidic metabolism and avoid some stresses.

Conclusion

At the end of this study, the pregnant women subjected to the test of the Oral Glucose Tolerance Test (OGTT) between 2013 and 2016 in consultation at the Pasteur Institute of Côte d'Ivoire (IPCI) were strongly predisposed to cardiovascular risks (CVR). Among the women, 77% did not present a return to the initial glycemia and presented glycemic anomalies. The statute of no return to the initial glycemia was more representative among old women from 30 to 40 years. For these last, the profile of the glycemia was higher than the normal profile of the glycemia after 30 minutes. Moreover, 86.67% consulted women had an abnormal HP without return to the initial glycemia. These women are predisposed with one occurred of diabetes and later at the cardiovascular risks. OGTT is thus a test with advising with the pregnant women for whom the cardiovascular risks are more significant.

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References

- ADA (America Diabetes Association). Clinical Practice Recommendations, Position statement, Diagnosis and classification of diabetes mellitus. Diabet Care 2010 ; 1: 2-69.
- Corati A. Déterminer le lien entre hyperglycémie et/ou hypoinsulinémie et la dégradation clinique observée avant le diagnostic du diabète associé à la fibrose kystique, Thèse de Doctorat de l'Université de Montréal, Canada 2015 ; 246 p.
- Scheen AJ., Luyckx FH. L'hyperglycémie provoquée par voie orale (HPO) revisitée. 1ère partie : Tolérance au glucose, diabète gestationnel et hypoglycémie réactive Méd Métab 2010 ; 5: 569-573.
- Luyckx FH., Scheen AJ. L'hyperglycémie provoquée par voie orale. Etude de la sécrétion, de la clairance et de l'action de l'insuline, et du rétrocontrôle par les hormones de la contre-régulation Immuno Biol Spéc 2003 ; 18: 185-190.
- Scheen A. J. . Evaluation de l'insulinosécrétion et de l'insulinosensibilité chez l'homme Thérap 2007 ; 62: 311-319.
- Scheen A. J. Evaluation de l'insulinosécrétion. In: Traitement du diabétologie, 2nd edition (ED: Grimaldi A.). Medicine-Sciences Flammarion, Paris, France 2009 98-109.
- Rohowij A. Hyperglycémie provoquée par voie orale: Etude d'interprétabilité des courbes plates au cours de la grossesse, A propos de 83 patientes suivies à la maternité régionale de Nancy, Thèse de Doctorat Médecine de l'Université de Lorraine, France 2012 ; 96 p.
- Abodo J. Rapport bilan d'activité de l'Association Obésité et Diabète de Côte d'Ivoire (AODCI) et plan d'action 2009-2018, 58 p..
- Sernyak MJ., Leslie DL., Alarcon RD. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. Am J Psychiatry 2002; 159: 561-566.

- LefèbvrePJ.,Scheen AJ. The postprandial state and risk of cardiovascular disease. *Diabetic Med* 1998; 15: 63-68.
- Coutinho M., Gerstein HC., Wang Y., Yusuf S. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care* 1999; 22: 233-240.
- Valensi P., Cosson E. Hemodynamic changes in postprandial state. *Diabetes Metab* 2006; 32 (2): 2-37.
- Smith NL, Barzilay JI, Shaffer D. Fasting and 2 hour postchallenge serum glucose measures and risk of incident cardiovascular events in the elderly: the Cardiovascular Health Study. *Arch Intern Med* 2002 ; 162: 209-216.
- Drouin P., Blickle J, Charbonnel B, Eschwege E, Guillausseau P., Plouin P., Daninos J, Balarac NR &Sauvanet J.
- Diagnostic et classification du diabète sucré les nouveaux critères. Rapport des experts de l'ALFEDIAM, *Diabet&Metab*1999 ; 25: 72-83
- Luyckx FH.,Scheen AJ. L'hyperglycémie provoquée par voie orale. Etude de la sécrétion, de la clairance et de l'action de l'insuline, et du rétrocontrôle par les hormones de la contre-régulation. *ImmunoBiolSpéc* 2003; 18: 185-190.
- Ader M., Pacini G., Yang YJ., Bergman RN. Importance of glucose per se to intravenous glucose tolerance. Comparison of the minimal-model prediction with direct measurements. *Diabetes* 1985; 34:1092-1103
- Capeau J. Transport of glucose in the cells: Physiology and pathology metabolism of the glucides and its methods of exploration at the man, cellular laboratory of biology, Faculty of Medicine Saint-Anthony, 27, street Chaligney, 75571 Paris cedex 12 France, *endocrinology-nutrition* 1997; (10-361-a-10).
- Austin M. & Edwards K. Small, dense low density lipoproteins, the insulin resistance syndrome and noninsulin dependent diabetes. *Curr Opin Lipidol* 1996; 7: 167-171.
- Meyer C., Stumvoll M., Nadkarni V., Dostou J., Mitrakou A., Gerich J. Abnormal renal and hepatic glucose metabolism in type 2 diabetes mellitus. *J Clin Invest* 1998 ; 102: 619-624.
- Orban J.-C., Ichaï C, acute metabolic Complications métaboliques aiguës du diabète, Acute metabolic complications of diabetes mellitus. *Réanim*2008 ; 17: 761-767.
- Gourdy P. Diabète de type 2 et insuffisance rénale: une situation à haut risque cardiovasculaire! *Méd des Mal Métab* 2011; 5: 31-36.
- Agarwal MM.,Punnose J., Dhatt GS. Gestational diabetes: problems associated with the oral glucose tolerance test. *Diabetes Res Clin Pract*2004 ; 63, pp.73-74.
- Scheen A.J., Hert de M., Diabète sucré iatrogène: L'exemple des antipsychotiques atypiques. *Rev Med Liege*, 5: 455-460. LefèbvrePJ.,Scheen AJ. Glucose metabolism and the postprandial state. *Eur J Clin Invest* 1999; 29: 1-6.