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Contribution to the study of the importance of hormonal assessment in cases of gestational diabetes

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Summary

Hormonal assessment is crucial in cases of gestational diabetes to evaluate pancreatic function. Gestational diabetes is often associated with insulin resistance. A hormone test measures insulin levels and assesses the pancreas ability to produce this essential hormone for blood sugar regulation. Monitoring hormones such as TSH (Thyroid-Stimulating-Hormone), c-peptide and prolactin can influence insulin sensitivity. A hormone profile can detect any hormonal imbalances that may contribute to the development of gestational diabetes, and help guide the treatment and management of this condition.

In Tebessa , a study was conducted on a population divided into three groups (women with gestational diabetes, non-diabetic pregnant women and a control group), to perform hormonal assessments of the following biochemical and immunological parameters (Glycemia, HbA1c, Peptide-c, Prolactin, Insulin, TSH, OGTT).

According to the results of our statistical study, a highly significant difference was observed between the TSH, Glycemia and Prolactin levels of patients with gestational diabetes compared to controls .

To sum up, hormonal assessment in gestational diabetes is essential for optimal management of the condition, prevention of complications and long-term monitoring of mother and child, as well as preventing complications related to gestational diabetes.

Key words: Gestational diabetes, Hormonal assessment, Insulin,Pregnant women,The pancreas

Résumé

Le bilan hormonal est crucial en cas de diabète gestationnel pour l'évaluation de la fonction Pancréatique : Le diabète gestationnel est souvent lié à une résistance à l'insuline. Un bilan hormonal permet de mesurer les niveaux d'insuline et d'évaluer la capacité du pancréas à produire cette hormone essentielle pour la régulation de la glycémie. Et la suivi des Hormones telles que TSH, peptide c, prolactine peuvent influencer la sensibilité à l'insuline. Le bilan hormonale permet de détecter d'éventuels déséquilibres hormonaux qui peuvent contribuer au développement di diabète gestationnel et aider à guider le traitement et la gestion de cette condition.

Dans la région de Tebessa on a fait une étude sur une population de trois groupes (des Femmes qui atteint le diabète gestationnel, des Femmes enceintes non-diabétique et groupe de témoins) , pour l'accomplir des bilans hormonales de différents paramètres biochimiques et immunologiques suivantes (Glycémie, HbA1c, Peptide-c, Prolactine, Insuline, TSH , HGPO).

D'après les résultats de notre étude statistique, une différence très hautement significative entre le taux de TSH, Glycémie, Prolactine des patients atteints le diabète gestationnel comparait aux témoins.

En résumé, le bilan hormonal en cas de diabète gestationnel est essentiel pour une gestion optimale de la condition, la prévention des complications et le suivi à long terme de la mère et de l'enfant, ainsi que pour prévenir les complications liées au diabète gestationnel.

Les mots clée: Diabète gestationnel, Bilan hormonal, Insuline, Femmes enceintes, Le pancréas

ملخص

يُعد التقييم الهرموني أمراً بالغ الأهمية في حالات سكري الحمل لتقييم وظيفة البنكرياس. غالبًا ما يرتبط سكري الحمل بمقاومة الأنسولين. يقيس اختبار الهرمونات مستويات الأنسولين ويقيّم قدرة البنكرياس على إنتاج هذا الهرمون الأساسي لتنظيم سكر الدم. ويمكن أن تؤثر مراقبة الهرمونات مثل الهرمون المنبه للهرمون المنبه للهرمون المنبه للهرمون المنبه للهرمون المنبه للهرمونات، والببتيد ج والبرولاكتين على حساسية الأنسولين. يمكن أن يكشف فحص الهرمونات عن أي اختلالات هرمونية قد تساهم في تطور سكري الحمل، ويساعد في توجيه علاج هذه الحالة وإدارتها..

في منطقة تبسة، أُجريت دراسة على مجموعة من ثلاث مجموعات نساء مصابات بسكري الحمل، ونساء حوامل غير مصابات بالسكري، ومجموعة مراقبةلإجراء التقييمات الهرمونية للمعايير الكيميائية الحيوية والمناعية التالية (جلوكوز الدم، البرولاكتين، الأنسولين،الهرمون المحفز للغدة الدرقية) .

ووفقًا لنتائج دراستنا الإحصائية، كان هناك فرق كبير للغاية بين مستويات الهرمون المنبه للسكري الحملي والسكر في الدم والبرولاكتين لدى مرضى سكري الحمل مقارنةً بالضوابط..

وخلاصة القول، يُعد التقييم الهرموني في حالات سكري الحمل ضرورياً للإدارة المثلى للحالة والوقاية من المضاعفات ومراقبة الأم والطفل على المدى الطويل، فضلاً عن الوقاية من المضاعفات المرتبطة بسكري الحمل..

الكلمات المفتاحية : سكري الحمل ، التقييم الهرموني ، الانسولين.النساء الحوامل، البنكرياس

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In this moment of gratitude, we turn first to Allah the source of all strength and inspiration. It is with humility that we acknowledge his benevolence in granting us the determination, patience, and perseverance necessary to complete this work.

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Thank you.

DEDICATION

To my dear parents Abdellaatif and Laila

your unwavering support and love have been my guiding light throughout this journey. Your belief in me has given me the strength to reach this milestone. I am forever grateful for all the sacrifices you've made to see me succeed. Thanks for being my rock and my inspiration.

To my beloved sisters, Ikram and Arwa

Ikram *your support and love have always been the source of my strength and optimism.*

Arwa *your laughter, kindness, and endless curiosity inspire me every day*

To my brothers, Chihab and Taki

You are my strength and my confidants, Thank you for being my pillars of support.

To my grandmother, Tourkia and Beya

You are the pillars of our family, the keepers of our traditions, and the embodiment of love and wisdom. Your presence in our lives brings warmth and light to our hearts.

To my aunts, Saida, Nedjma, Nacira, Halima and Rahma

you are the shining stars in our family, radiating love, kindness, and strength.

My dear friends, Ibtissam, Chaima, dhikra, oumaima

Lamia, Alaa, Kouka…

you are the heart and soul of this wonderful friendship. I am grateful for every moment we've spent together.

My dear colleague Hadjer

I value the partnership we share and the experiences we've had together. Thank you for being an amazing companion.

AOUIMEUR Rihab

DEDICATION

I dedicate this work to :

My dear parents

No dedication, no words could adequately express the gratitude and love i have for you. Thank you for every moment you spent with me. Your support and encouragment have always given me the strengh to persevere and thrive in life.

My dear sister Sarah

I love you so much, thank you for illuminating the path of my studies and for always being by my side, thank you for always providing me with positive energy. Maty god keep you for me and grant you health and hapiness.

My dear friends

Thank you for your love and for being with me in difficult times and adversity.

GHELLAB Hadjer

Figures list :

Tables list

Abreviationslist :

Abreviations	*Designation*
GD	Gestational Diabetes
TSH	Thyroid-stimulating hormone
OGTT	Oral glucodetolerance test
HbA1c	Hemoglobin type A separated on cation exchange chromatography
BMI	Body mass index
HHS	hyperosmolar hyperglycemic state
LDL	Low-density lipoprotein
HDL	High-density lipoprotein
hPL	Human placental lactogen
hCG	Human chorionic gonadotropin
CRH	Corticotropin-releasing hormone
HPA	Hypothalamic-pituitary-adernal axis
GH	Growth hormone
FSH	Follicle-stimulating hormone
LH	Luteinizing hormone
T4	Thyroxine
T3	Triiodothyronine
C-peptide	Connecting peptide

Contents

Chapter III: Hormonal Tests

Experimental part

Bibliographical synthesis

Introduction

Diabetes is a chronic metabolic disorder characterized by persistent hyperglycemia, resulting either from insufficient insulin production by the pancreas or from the ineffective utilization of insulin by the body. There are several types of diabetes, with the principal forms being Type 1 diabetes, Type 2 diabetes, and gestational diabetes **(Atlas, 2015)**

Gestational diabetes is a form of diabetes that occurs during pregnancy in women who were not previously diabetic. This condition arises due to specific hormonal and metabolic changes associated with pregnancy, leading to increased insulin resistance, it presents significant risks for both the mother and the child, including complications at birth and a heightened predisposition to Type 2 diabetes later in life **(Momo *et al.*, 2021)**

Hormonal changes during pregnancy play a central role in the development of gestational diabetes. Hormones such as placental lactogen, cortisol, TSH, and prolactin alter the body's sensitivity to insulin, thereby contributing to hyperglycemia. These hormonal alterations necessitate rigorous monitoring to effectively prevent and manage associated complications **(Barras & Héritier., 2011)**

The importance of hormonal assessment in cases of gestational diabetes is crucial. A thorough hormonal evaluation not only facilitates the early diagnosis of this condition but also aids in tailoring therapeutic strategies to ensure the health of both the mother and the child. Indeed, the proper management of gestational diabetes relies on a precise understanding of the hormonal and metabolic interactions involved, thereby minimizing risks and optimizing obstetric outcomes.**(Berdah, 2010)**

In our research, we aim to explore the intricate interplay between hormonal changes and gestational diabetes, with a particular focus on novel biomarkers and advanced assessment techniques. Through longitudinal studies tracking hormonal trajectories throughout pregnancy, we aim to elucidate how these changes vary among different populations and their implications for maternal health. By evaluating the effectiveness of targeted interventions aimed at modulating hormonal pathways implicated in gestational diabetes, we aspire to enhance the management and outcomes of this condition.

Our work aims to explore the generalities of diabetes, delve into the understanding of gestational diabetes and its accompanying hormonal changes, and highlight the significance of hormonal assessment in the management of gestational diabetes.

Chapter I:
Diabetes

1. Generality

When unnatural chemical reactions interfere with metabolic processes, when there is a loss of enzymes or hormones essential for necessary chemical reactions, or in the case of liver disease, pancreas, adrenal glands, or other organs involved in metabolism, it leads to metabolic disorders.

Metabolic diseases are a group of disorders that result from the absence or dysfunction of certain enzymes required for metabolic reactions in the cell. Diabetes is one of the most common metabolic diseases. It is characterised by the body's inability to regulate blood glucose levels correctly, which can lead to serious long-term complications.**(Lotfy *et al.*, 2017).**

2. Definition

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesn't make enough insulin. In the past three decades the prevalence of type 2 diabetes has risen dramatically in countries of all income levels. Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin by itself.

For people living with diabetes, access to affordable treatment, including insulin, is critical to their survival**. (World health organization)**

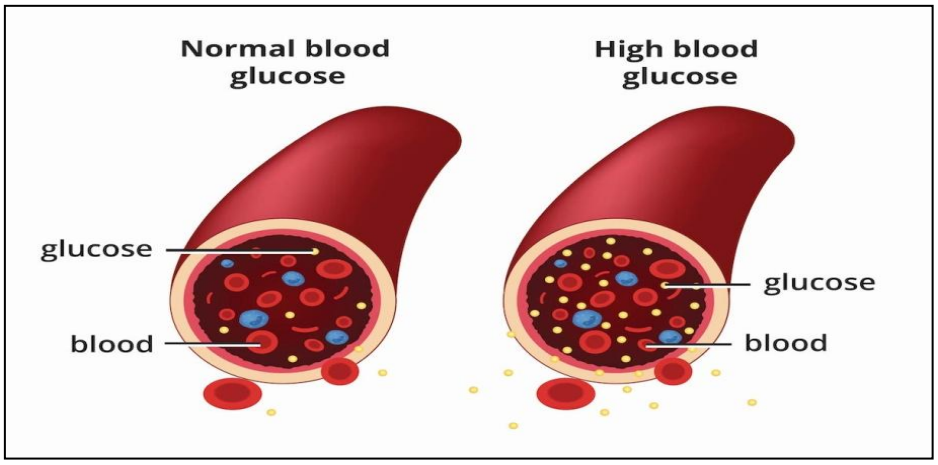

Figure 01: Illustration of the excessive rise in blood glucose levels **(Soufiane adjana, 2022)**

3. Classification

3.1. Type 1 diabetes

Type 1 diabetes is caused by the destruction of β-cells , typically leading to an absolute insulin deficiency. Usually, the destruction of β-cells is an immune-mediated process (identified as type 1A), but a small group of cases present with an idiopathic form of the disease (identified as type 1B). The classic clinical features of type 1 cases include abrupt onset at a young age, before the age of 35, normal body mass index (BMI), and high risk of diabetic ketoacidosis.

This form of diabetes accounts for 5-10% of diabetes cases.**(Dimeglio *et al.*, 2018)**

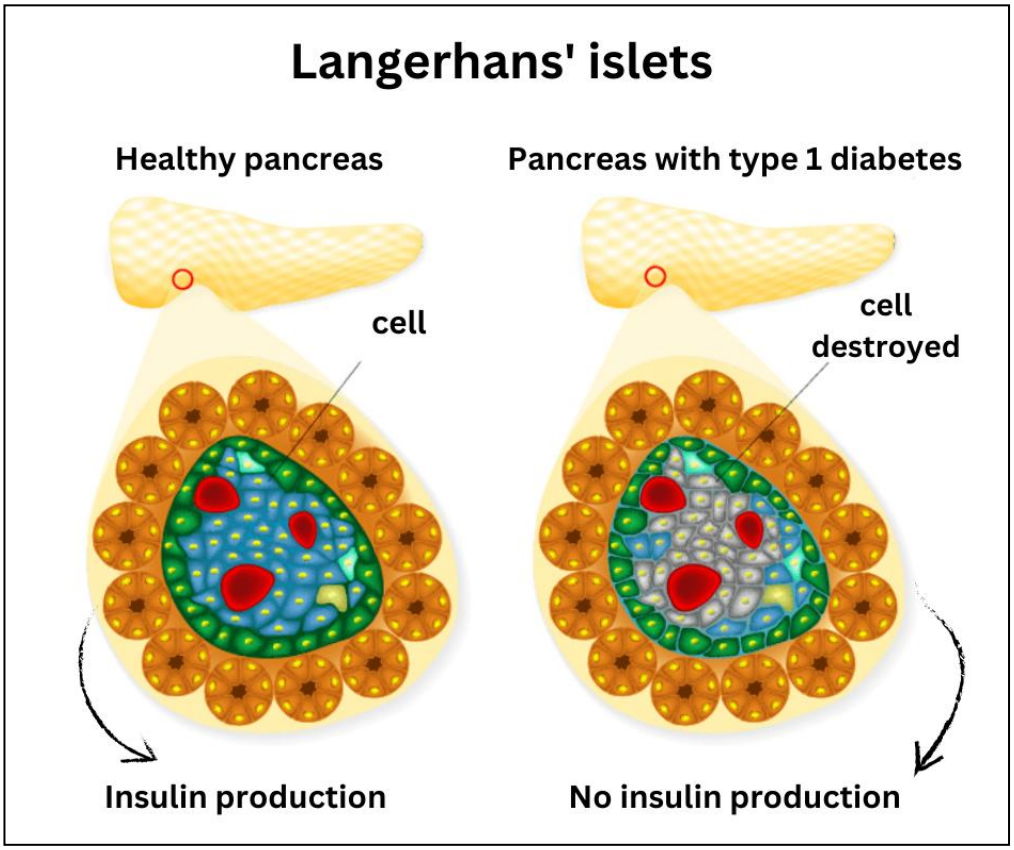

Figure 02:The difference between a healthy pancreatic cell and a type 1 diabetes cell **(FRED, 2022).**

3.2. Type 2 diabetes:

Type 2 diabetes is due to cells dysfunction leading to progressive loss of insulin secretion against a background of insulin resistance**(Chatterjee *et al.*, 2017).** Type 2 diabetes differs greatly from type 1 in terms of clinical characteristics (features), as the onset of the disease is slow and generally at a later age. Most cases are overweight. Generally do not develop with ketoacidosis. It represents between 90 and 95% of diabetes cases**(Defronzo *et al.*, 2015).**

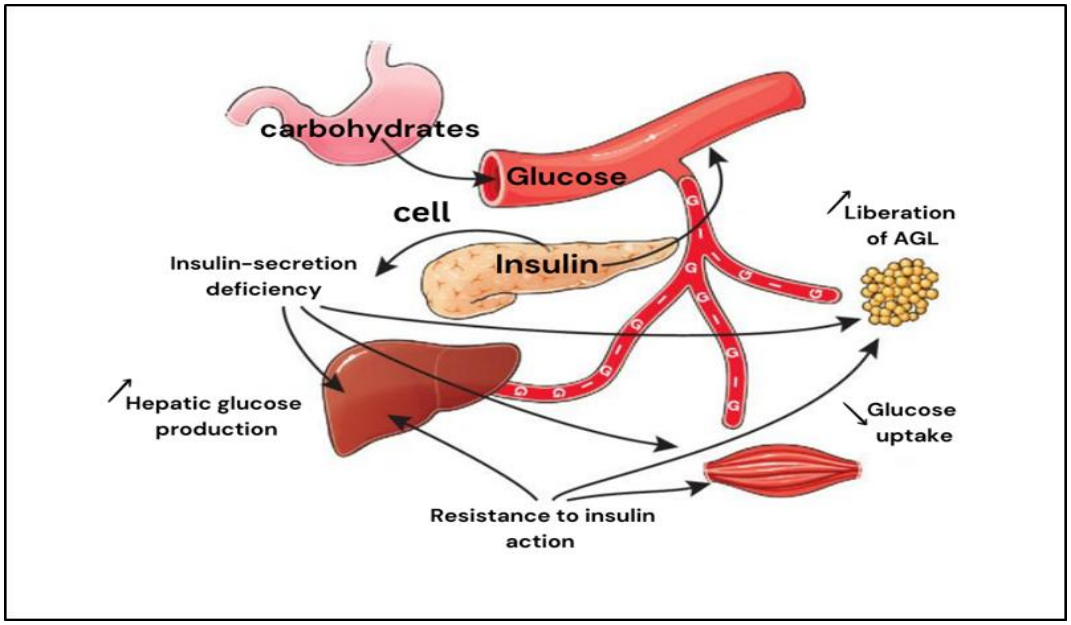

Figure 03: Schematic representation the impact of abnormal insulin secretion and insulin sensitivity in type 2 diabetes **(Colette & Monnier , 2014).**

3.3. Gestational diabetes:

Gestational diabetes (GD) (is defined as glucose intolerance occurring during pregnancy)is a type of diabetes diagnosed during pregnancy, usually during the second or third trimester, in women who had not previously been diagnosed with diabetes**(Mack & Tomich., 2017).**

Typically, Gestational diabetes does not persist after childbirth, but some cases of type 2 diabetes are discovered after the post-partum period.

Being overweight, advanced age, family history of diabetes or personal history of GD are the most common risk factors **(McIntyre *et al.*, 2019).**

4. Symptoms

The classic symptoms of diabetes include polyuria, polydipsia, fatigue and weakness.Type 1 diabetic patients also experience weight loss despite an increased appetite, and sometimes blurred vision. In type 1 diabetes, symptoms typically develop over a few days or weeks; so cases are unlikely to be diagnosed as a result of routine medical screening. However, the onset of type 2 diabetes is often not associated with clinical signs, so patients are usually diagnosed during a routine check-up. In addition to the classic symptoms of diabetes, cases of type 2 may also present with other conditions such as nephropathic **(Ramachandran, 2014).**

5. Complications of diabetes

5.1. Acute complications

- **Hypoglycemia:**

This is a frequent and unpleasant complication, occurring most often in type 1 diabetics, and can lead to a hypoglycemic coma **(Papatheodorou *et al.*, 2016).**

- **Acidosis:**

Diabetic ketoacidosis is one of the most severe acute complications of diabetes. diabetes, which can lead to coma and even death, this result from insulin deficiency, leading to an accumulation of ketone bodies toxic chemical substances, which are responsible for metabolic acidification, which is the cause of the clinical signs **(Papatheodorou *et al.*, 2018).**

- **Hyperosmolar coma:**

Hyperosmolar coma, also known as hyperosmolar hyperglycemic state (HHS), is a serious medical condition characterized by extremely high blood sugar levels (hyperglycemia), severe dehydration, and altered mental status leading to coma. This condition typically occurs in people with type 2 diabetes mellitus, often due to a

combination of factors such as illness, infection, inadequate fluid intake, insufficient insulin, or neglect of treatment **(Pasquel & Umpierrez., 2014).**

The hyperosmolar coma is considered a medical emergency and requires immediate treatment, usually involving intravenous fluids to correct dehydration, insulin therapy to lower blood sugar levels, and addressing any underlying medical conditions that mayhave triggered the episode. Without prompt intervention, hyperosmolar coma can lead to severe complications and even death **(Rosenbloom, 2010).**

- **Lactic acidosis:**

Lactic acidosis is defined as a clinical and metabolic picture of severe acidosis resulting from an accumulation of lactic acids in the body. It is a rare severe prognosis, with an estimated mortality rate of 50% **(Kraut & Madias., 2014).**

5.2. Chronic complications

The long-term complications of diabetes are classically divided into two categories:

- **Microangiopathic complications:**

Damage to blood vessels caused by increased blood sugar levels.This can lead to complications such as diabetic retinopathy (eye damage), diabetic nephropathy (kidney damage), and diabetic neuropathy (nerve damage) **(Lotfy *et al.*, 2017).**

- **Macroangiopathic complications:**

Cardiovascular disease, It combines two arterial pathologies - atherosclerosis and arteriosclerosis - and can be clinically manifested by strokes, myocardial ischaemia , heart failure and arteritis of the lower limbs **(Fowler, 2011).**

6. Diabetes risk factors

The risk factors for diabetes can be divided into two main categories: non-modifiable risk factors and modifiable risk factors. Here is a list of the main risk factors associated with diabetes:

6.1. Non-modifiable risk factors

- **Family history of diabetes:** The risk of developing type 2 diabetes is higher in people who have family members (parents, brothers, sisters) with diabetes.
- **Age:** The risk of developing diabetes increases with age, particularly after the age of 45.
- **Ethnic origin:** Certain ethnic groups, such as African-Americans, Hispanics, Native Americans, Asians and Pacific Islanders, have an increased risk of diabetes.
- **History of gestational diabetes:** Women who have had gestational diabetes during pregnancy have an increased risk of developing type 2 diabetes later in life **(Williams *et al.*, 2017).**

6.2. Modifiable risk factors

- **Overweight and obesity:** Excess weight, particularly the accumulation of abdominal fat, is a major risk factor for type 2 diabetes.
- **Sedentary lifestyle:** A sedentary lifestyle, characterized by a lack of physical exercise, increases the risk of diabetes **(Stringhini *et al.*, 2012).**
- **Unbalanced diet:** A diet high in calories, saturated fats and sugars and low in fibre can contribute to the development of diabetes.
- **High blood pressure:** High blood pressure is often associated with diabetes and increases the risk of complications **(Spencer *et al.*, 2008).**
- **High cholesterol:** High levels of LDL ('bad') cholesterol and low levels of HDL ('good') cholesterol can increase the risk of diabetes and cardiovascular disease.
- **Smoking:** Smoking is a risk factor for many health problems, including type 2 diabetes.

Reducing modifiable risk factors through a healthy lifestyle, including a balanced diet,regular physical activity and stopping smoking, can help prevent or delay the development of diabetes **(Hackett & Steptoe., 2017).**

Chapter II:
Gestational diabetes

1. Definition

Gestational diabetes is a worldwide public health problem, it's defined as glucose intolerance during pregnancy. Gestational diabetes and metabolic syndrome are two major metabolic illnesses that affect women all over the world, Furthermore, gestational diabetes has been reported that it is one of the first abnormalities to be detected during the development of metabolic syndrome. The prevalence is increasing due to delayed motherhood and unhealthy lifestyles, Gestational diabetes leads to fetus hyperglycemia, which in turn causes hyperinsulinemia, the body goes through other changes such as weight gain "obesity", These changes cause your body's cells to use insulin less effectively " a condition called insulin resistance" Since insulin acts as a growth hormone during pregnancy, this will induce macrosomia-related perinatal adverse outcomes, These hormonal changes can lead to high blood sugar and diabetes after delivery **(Catalano, 2014).**

2. Etiology of Gestational Diabetes

Gestational diabetes is the most common metabolic disturbance during pregnancy. The etiology of gestational is related to :

• The pancreatic beta-cell dysfunction or the delayed response of the beta cells to glycemic levels

• The marked insulin resistance resulting from placental hormonal release **(Johns *et al.*, 2018).**

The placenta is a highly active endocrine organ during gestation, it plays a critical role in the development of gestational insulin resistance secreting a series of pregnancy-specific hormones called " placental hormones" e.g Human placental lactogen " hPL" Human chorionic gonadotropin "hCG", steroid hormones "Cortisol" and Human placental growth hormones "Prolactin, Progesterone, Corticotropin-releasing-hormone CRH" **(Melamed *et al.*, 2008).**

The human placental lactogen it's the main hormone released by the placenta related to increased insulin resistance and it's capable of provoking alterations in the insulin receptors in gestational diabetes, the second placental hormone is Human chorionic gonadotropin hCG is a hormone produced primarily by the placenta during pregnancy.

Human placental lactogen (hPL) is the primary hormone released by the placenta, associated with increased insulin resistance. It can alter insulin receptors in gestational diabetes. Human chorionic gonadotropin (hCG) is another placental hormone that serves as a marker of placental function and stimulates the maternal thyroid gland. Maternal thyroid function influences gestational diabetes pathophysiology. Additionally, hCG stimulates the corpus luteum to produce progesterone, prolactin, and corticotropin-releasing hormone (CRH). These hormones contribute to insulin resistance and hyperglycemia during pregnancy. Maternal hyperglycemia crosses the placenta, leading to fetal hyperglycemia and increased fetal tissue growth. Higher body mass index may induce chronic inflammation, leading to the synthesis of Xanthurenic acid associated with pre-diabetes and gestational diabetes. As the placenta grows, the risk of insulin resistance increases due to the production of these hormones, leading to a blocking effect on insulin, known as the contra-insulin effect. Cortisol, a steroid hormone, also plays a crucial role in hyperglycemia and fetal development in gestational diabetes by influencing lipid metabolism and distribution. Other hormones like growth hormone, prolactin, progesterone, and CRH, upregulated by cortisol, further contribute to insulin resistance and hyperglycemia during pregnancy **(Dirar & Doupis., 2017).**

Cortisol directly:

- Promotes hyperglycemia through induction of hepatic genes responsible for gluconeogenesis
- Increases skeletal muscle insulin resistance through inhibition of glucose transporter GLUT 4 translocation to the cell surface **(Chiefari *et al.*, 2017).**

High level of serum this hormone leads to central lipid accumulation, resulting insulin resistance and indirectly through activation of fetal hypothalamus-pituitary-adernal HPA axis. Increased cortisol during pregnancy increases the antagonism of insulin action.**(Melamed *et al.*, 2008).**

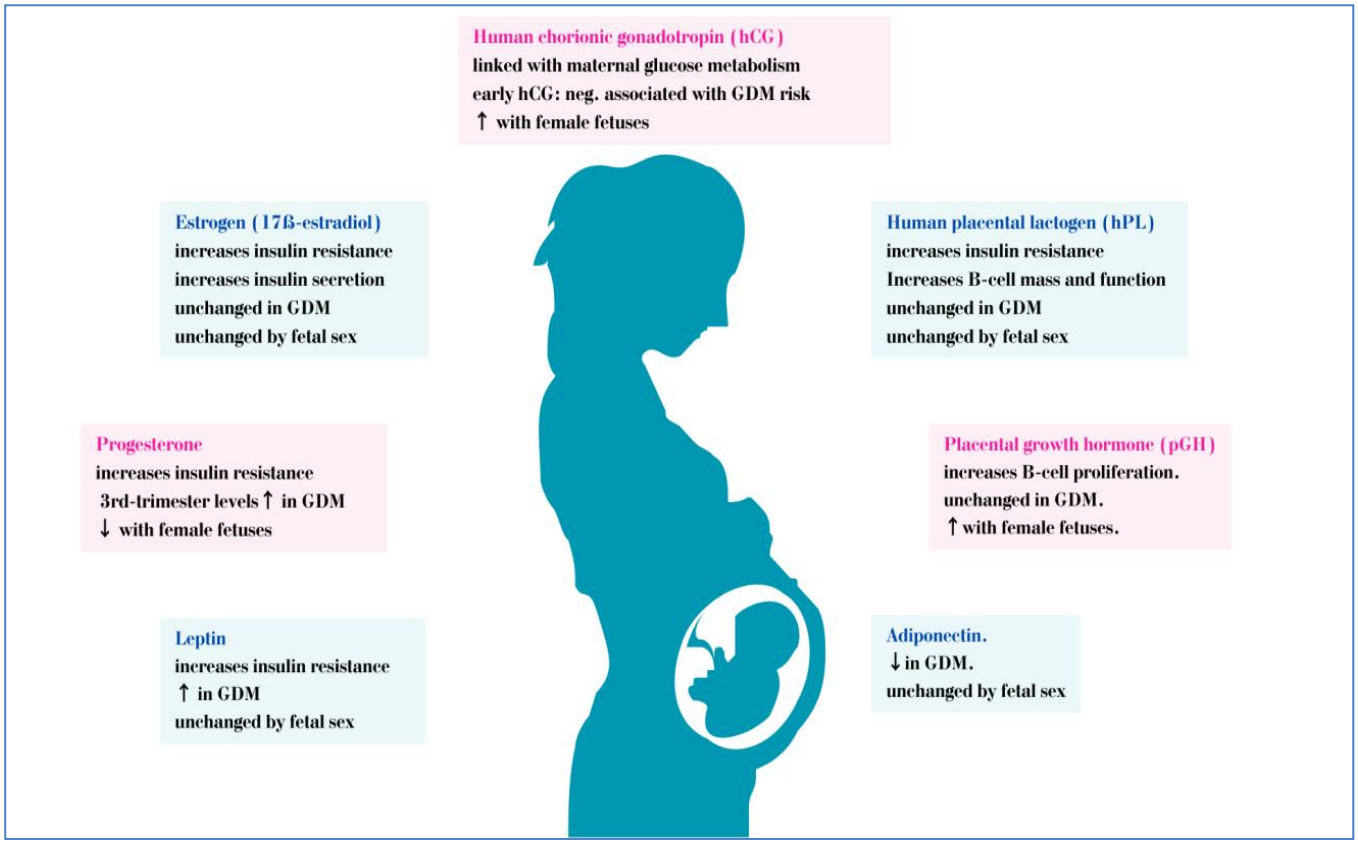

Figure 04: The hormones secreted by the placenta **(Personal design, 2024).**

3. Complications

The risks of multiple serious prenatal complications are increased in women with gestational diabetes including gestational hyperglycemia which is associated with a well documented range of adverse pregnancy outcomes for the mother and fetus ,The complications of developing gestational diabetes categorize as maternal and fetal **(Jain *et al.*, 2014).**

The maternal complication: hypertension, preeclampsia, increased risk of developing diabetes and increased risk of cesarean delivery **(Bener *et al.*, 2014).**

The fetus complication: macrosomia, neonatal hypoglycemia, neonatal respiratory distress syndrome, increased perinatal mortality and hypocalcemia **(Reece, 2010).**

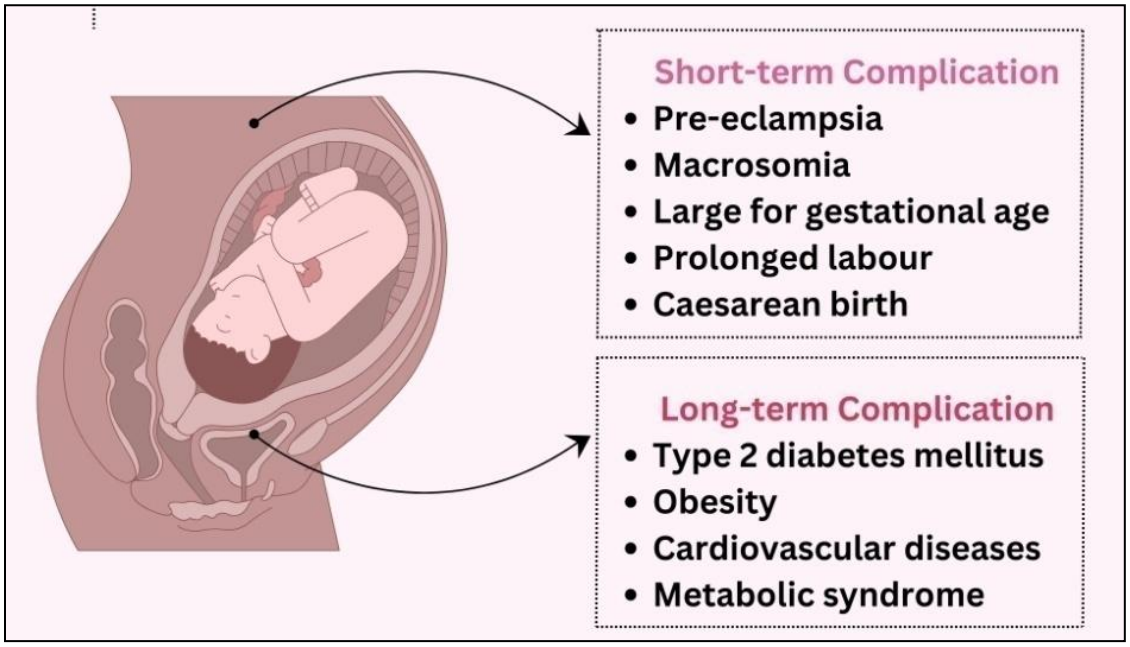

Figure 05: Short and long-term gestational diabetes complication **(Personal design, 2024).**

4. Screening for Gestational Diabetes

During the first antenatal appointment " Booking appointment " at around week 8 to 12 of the pregnancy , The midwife or the doctor will ask you some questions to determine whether you are at increased risk of gestational diabetes, If you have 1 or more risk factors for gestational diabetes a screening test should be offered, The screening test is called an oral glucose tolerance test « OGTT », which take about 2 hours, it involves having a blood test in the morning, when you have not had any food or drink for 8 to 10 hours, You are then given a glucose drink, after resting for 2 hours another blood sample is taken to see how your body is dealing with the glucose, The OGTT is done when you are between 24 and 28 weeks pregnant ,If you have had gestational diabetes before you will be offered an OGTT earlier soon after the booking appointment, then another OGTT at 24 to 28 weeks if the first test is normal **(Hillier *et al.*, 2008).**

5. Treatment for Gestational Diabetes

Gestational diabetes can classify as Gestational diabetes managed without medication and responsive to nutritional therapy is diet-controlled gestational diabetes, On the other side, It's managed with medication to achieve adequate glycemic control women with gestational diabetes must take insulin" if it is ordered by the doctor **(Farrar *et al.*, 2017).**

Gestational diabetes is characterized by insulin resistance which leads to hyperglycemia and its negative effects on fetus growth, pregnant women with gestational diabetes are initially managed with medical nutrition therapy and light exercise. Insulin has generally been recognized as the first-line drug because it is effective and does not cross the placenta it has a great fetus safety profile, it attaint tight maternal glucose control and is therefore recommended as a gold standard for treatement. Other treatement strategies, oral antidiabetic drugs such as metformin or glyburide, have been used in recent years given that insulin therapy has several downsides in gestational diabetes.

Fortunately, metformin is not associated with fetus abnormalities when used during the first trimester of pregnancy (**Gilbert *et al.*, 2006)**, in addition, metformin appears to be safe in the second and third trimester of pregnancy **(Johns *et al.*, 2018).**

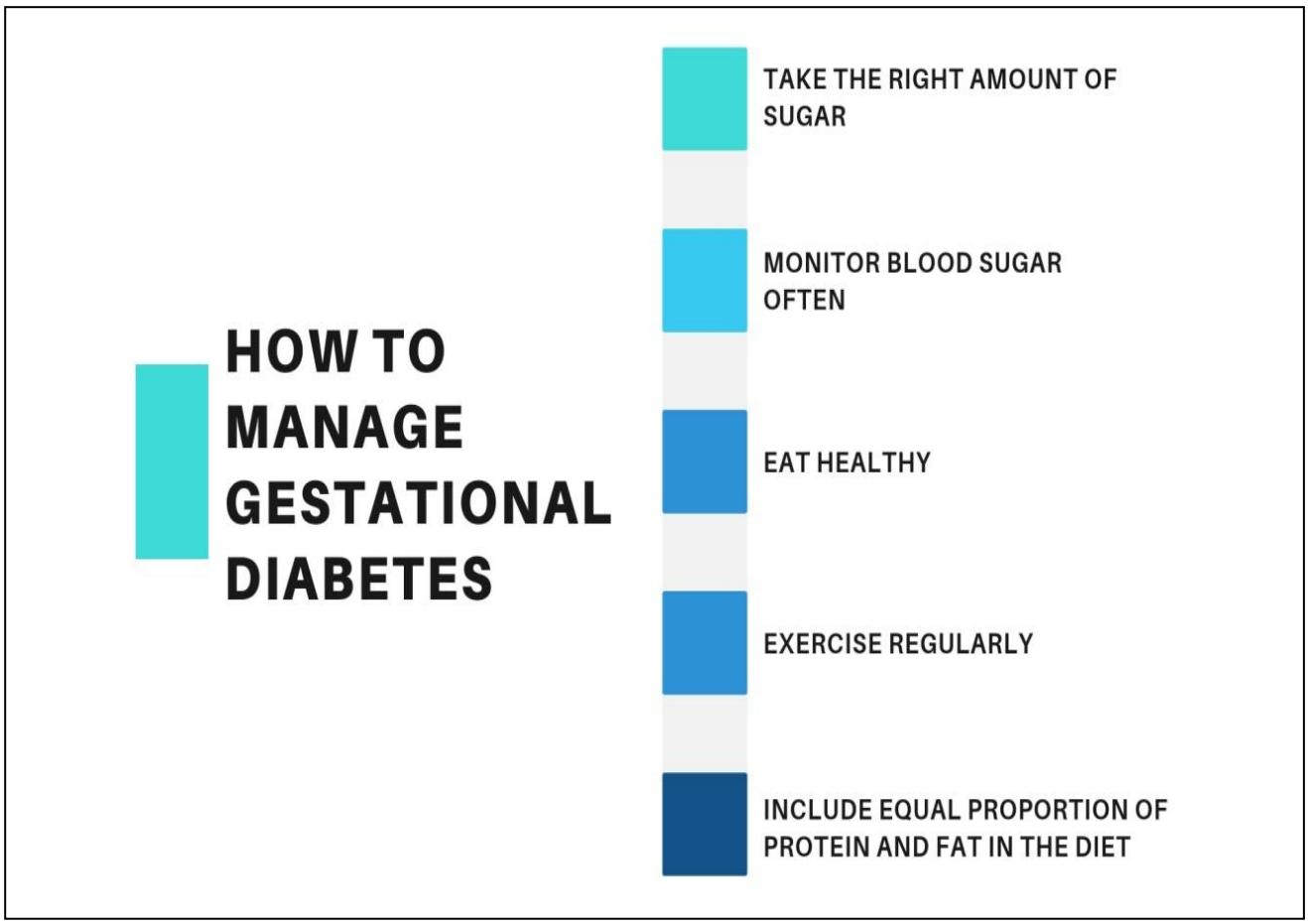

Figure 06: Appoaches for managing gestational diabetes **(Personal design, 2024).**

Chapter III:
Hormonal Tests

1. Generality

The endocrine system is a complex network of glands and organs that produce and release hormones into the bloodstream. The main endocrine glands include the pituitary, thyroid, adrenal, pancreas, and ovaries. These glands work together to maintain the hormonal balance necessary for the body to function correctly **(Didimo, 2009).**

The hormonal system is made up of a group of glands and organs that regulate and control different body functions through the production and secretion of hormones **(Estaquier *et al.*, 2021).**

Hormones are chemical substances produced by the endocrine glands and released into the bloodstream to act on target cells at a distance. They regulate numerous physiological processes such as growth, metabolism, reproduction, and stress. Each hormone has a specific role in the body, acting as a chemical messenger to coordinate and control various functions **(Castinetti *et al.*, 2008).**

2. Hormones and their role

2.1. Growth hormone (GH): is a peptide hormone produced by the anterior pituitary gland. It plays a crucial role in growth, fat and sugar metabolism, and tissue regeneration. GH stimulates growth by promoting cell multiplication and increasing cell size and helps maintain muscle mass, bone density, and healthy connective tissue **(Goldfarb, 2023).**

2.2. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH): Produced by the pituitary gland, these hormones regulate the menstrual cycle and the release of eggs by the ovaries **(Al-Saiady *et al.*, 2015).**

2.3. TSH (Thyroid Stimulating Hormone): is a hormone produced by the pituitary gland. It has a crucial role in regulating the thyroid gland. TSH stimulates the production and release of thyroid hormones, thyroxine (T4) and triiodothyronine (T3), by the thyroid gland **(Fast *et al.*, 2011).**

2.4. Prolactin: is a peptide hormone produced by the anterior pituitary gland in the brain. Its main role is to stimulate milk production in mammals. In pregnant and breastfeeding women, prolactin is essential for initiating and maintaining lactation after childbirth **(Delemer, 2009).**

2.5. Estrogens: Produced mainly by the ovaries, estrogens are responsible for the development of female secondary sexual characteristics, controlling the menstrual cycle, and regulating fertility **(Dragin *et al.*, 2016).**

2.6. Progesterone: Progesterone is a steroid hormone produced mainly by the corpus luteum in the ovaries in women. It plays a crucial role in the menstrual cycle and pregnancy **(Lollivier *et al* .,2014).**

2.7. Insulin and glucagon: are two key hormones in the regulation of blood sugar levels.

- **Insulin:** Insulin is a hormone produced by the beta cells of the islets of Langerhans in the pancreas. Its main role is to lower blood sugar levels by facilitating the absorption of glucose by the body's cells, where it is used as a source of energy or stored as glycogen in the liver and muscles. Insulin is released in response to a rise in blood sugar levels after a meal, and its action promotes the storage of glucose, bringing blood sugar levels back to normal **(Capeau, 2008).**

- **Glucagon:** Glucagon is a hormone produced by the alpha cells of the islets of Langerhans in the pancreas. Unlike insulin, glucagon's function is to raise blood glucose levels when blood glucose levels are low, such as during fasting or between meals. Glucagon stimulates the breakdown of glycogen stored in the liver into glucose, and it also encourages the liver to produce glucose (gluconeogenesis), thereby raising blood glucose levels **(Scheen, 2023).**

These hormones work together to regulate the menstrual cycle, pregnancy, childbirth, breastfeeding, and other physiological processes specific to women.

3. Hormonal changes in Gestational Diabetes

During pregnancy, a woman's body undergoes numerous hormonal changes to support the development and growth of the fetus, as well as to prepare the body for childbirth and breastfeeding. Also there are some of the main hormonal changes that occur during GD.

Gestational diabetes is a condition in which blood glucose levels rise during pregnancy in women who did not have diabetes before conception. Hormonal changes during pregnancy can contribute to the development of gestational diabetes in several ways.

3.1.Insulin secretion abnormality

Gestational diabetes is a condition in which blood sugar levels become elevated during pregnancy. This condition can occur when the body cannot produce enough insulin to meet the increased needs during pregnancy, resulting in hyperglycemia.

During pregnancy, there are functional and structural changes in the islets of Langerhans. Pregnancy is marked by a progressive increase in fasting insulin levels, with levels doubling between the beginning and end of pregnancy. The islets of Langerhans undergo structural and functional changes to adapt to the increase in insulin secretion. This involves hypertrophy and hyperplasia of the beta cells.

In addition, hyperinsulinism is reactive and predominantly postprandial. The peak plasma level is later in patients with gestational diabetes, due to the reduced sensitivity of the beta cells, which allows an early peak in insulin secretion. Insulin is broken down mainly in the liver. It is reduced in pregnant women, as a result of an adaptive phenomenon secondary to insulin resistance.

Abnormalities in insulin secretion, the production or release of insulin, can contribute to the development of gestational diabetes **(Olivesi, 2016)**

3.2. Increased insulin resistance

Insulin resistance is a factor in the development of gestational diabetes. During pregnancy, a woman's body undergoes significant hormonal changes that can lead to insulin resistance, meaning that the cells become less sensitive to the insulin produced by

the pancreas. This insulin resistance is exacerbated by the hormones secreted by the placenta and other hormones (TSH, prolactin, cortisol, FSH, LH, GH, Estrogen, and Progesterone...) to support the growth and development of the fetus.

Hepatic and muscular insulin resistance is physiological and progressive during pregnancy, it allows the glucose available to the fetus to be spared. The pancreas initially produces more insulin to compensate for this resistance, this adaptation may be insufficient, leading to an increase in blood sugar levels **(Olivesi, 2016).**

3.3. Hormones and gestational diabetes

a) **Estrogen:** is steroid hormone essential for many physiological processes, including the regulation of metabolism and pancreatic beta-cell function. During pregnancy, Estrogen levels increase considerably, which can have an impact on insulin sensitivity and the development of gestational diabetes.

The effects of estrogen on gestational diabetes:

- **Insulin resistance**: Estrogen can contribute to insulin resistance, which means that cells become less sensitive to the insulin produced by the pancreas. Increased insulin resistance is a feature of gestational diabetes.
- **Effects on pancreatic beta cell function:** Estrogens can affect the function of pancreatic beta cells, which are responsible for insulin production. High levels of estrogen can affect the ability of beta cells to secrete insulin in response to blood sugar.
- **Adiposity:** Oestrogens can influence the distribution of fat in the body. Increased adiposity, particularly an accumulation of abdominal fat, is a risk factor for insulin resistance and gestational diabetes **(Chevalier *et al.*, 2009).**

b) **Progesterone**: a steroid hormone produced in large quantities during pregnancy, may also play a role in gestational diabetes (GD).

- **Insulin resistance:** Studies suggest that progesterone may contribute to insulin resistance during pregnancy. Increased insulin resistance makes cells less sensitive

to the insulin produced by the pancreas, which can lead to increased blood glucose levels.

- **Effects on carbohydrate metabolism:** Progesterone may have direct effects on carbohydrate metabolism.
- **Interactions with other hormones:** Progesterone can interact with other hormones involved in the regulation of metabolism, such as insulin, estrogen, and counter insulin hormones. These complex interactions between hormones can influence insulin sensitivity and the development of GD.
- **Effects on pancreatic beta cell function:** Progesterone can also influence the function of pancreatic beta cells, which are responsible for insulin production. High levels of progesterone can potentially affect the ability of beta cells to secrete insulin in response to blood glucose **(Mehaoudi *et al.*, 2015).**

c) **Prolactin**: is a peptide hormone primarily known for its role in lactation and milk production in women. There is evidence that prolactin has effects on blood sugar regulation and a role in GDM.

- **Effects on metabolism:** Preclinical studies in animals and observational studies in humans have suggested that prolactin may influence carbohydrate metabolism. Elevated prolactin levels have been associated with impaired glucose tolerance and increased insulin resistance, which are features of gestational diabetes.
- **Interactions with other hormones:** Prolactin may interact with other hormones involved in the regulation of metabolism. These complex interactions between hormones may have effects on insulin sensitivity and the development of gestational diabetes.
- **Thyroid-prolactin axis hypothesis:** Some research suggests that there may be an interaction between the thyroid-prolactin axis and the development of gestational diabetes. Abnormalities in prolactin and thyroid regulation have been observed in women with gestational diabetes **(Weisnagel *et al.*, 2013)**

d) **TSH:** The relationship between thyroid-stimulating hormone (TSH) and gestational diabetes (GDM) is complex and requires careful evaluation.

- **Hypothyroidism and gestational diabetes:** Impaired thyroid function, including hypothyroidism (elevated TSH levels with normal levels of thyroid hormones T3 and T4), has been associated with an increased risk of gestational diabetes. Women with hypothyroidism during pregnancy may have insulin resistance and disturbances in carbohydrate metabolism, increasing the risk of gestational diabetes.
- **Effects of pregnancy on the thyroid:** During pregnancy, thyroid hormone requirements increase to meet increased metabolic demands. In some women, this can lead to changes in thyroid function, including fluctuations in TSH levels. Elevated TSH levels during pregnancy may indicate impaired thyroid function, which may influence the risk of gestational diabetes.
- **Inflammation and oxidative stress:** Studies have suggested that inflammation and oxidative stress, associated with high TSH levels, may contribute to the development of gestational diabetes. These processes may influence insulin resistance and carbohydrate metabolism during pregnancy.
- **Hormonal interactions:** TSH can interact with other hormones for the regulation of metabolism, such as thyroid hormones and counterinsulin hormones. These complex interactions between hormones affect insulin sensitivity and the development of gestational diabetes **(Pinto *et al.*, 2021)**

e) **Cortisol**: is a steroid hormone produced by the adrenal glands in response to stress and is involved in many metabolic and physiological processes in the body. There is a potential link between cortisol and gestational diabetes (GD), although the relationship is complex and multifactorial.

- **Insulin resistance:** Cortisol is known to induce insulin resistance, which means that cells become less sensitive to the insulin produced by the pancreas. Increased insulin resistance is a key factor in the development of gestational diabetes, as it leads to increased blood glucose levels.

- **Stress:** Cortisol is often called the stress hormone because its release is stimulated by physical and psychological stress. Stress during pregnancy can increase cortisol levels, which may have implications for blood sugar regulation and the development of gestational diabetes.

- **Interactions with other hormones:** Cortisol can interact with other hormones involved in regulating metabolism, such as insulin and thyroid hormones. These complex interactions between hormones can influence insulin sensitivity and the development of gestational diabetes**(Rogatien *et al*., 2023).**

f) **Human placental lactogen (HPL):** is a hormone produced by the placenta during pregnancy. Although its main role is to support the growth and development of the fetus, HPL can also have effects on maternal metabolism and play a role in gestational diabetes (GD).

- **Insulin resistance:** HPL is known to have similar effects to growth hormone, which can lead to insulin resistance in the mother during pregnancy. Insulin resistance makes cells less sensitive to the insulin produced by the pancreas, which can lead to increased blood glucose levels, a factor in the development of gestational diabetes.

- **Inhibition of insulin action:** In addition to inducing insulin resistance, HPL may also inhibit the action of insulin on target cells, further exacerbating insulin resistance and contributing to the development of gestational diabetes.

- **Interactions with other hormones:** HPL can interact with other hormones involved in the regulation of metabolism, such as insulin, thyroid hormones. These complex interactions between hormones can influence insulin sensitivity and the development of gestational diabetes **(Lacasse, 2013)**

4. The importance of a hormonal assessment in cases of gestational diabetes

Hormonal assessment plays an important role in the management of gestational diabetes (GD), as it helps to assess the hormonal imbalances that may contribute to the development of this condition.A hormonal assessment can help to identify the underlying hormonal imbalances that may contribute to the development of gestational diabetes. This may include hormones such as insulin, cortisol, thyroid hormones, sex hormones and other hormones involved in regulating metabolism. Also

known as Insulin Sensitivity Testing, hormone tests can help assess insulin sensitivity in women with gestational diabetes. This may include tests to measure levels of insulin, glucose and other metabolic markers that may indicate insulin resistance **(Djagadou *et al.*, 2019).**

Certain hormonal imbalances associated with gestational diabetes can also increase the risk of complications for both mother and baby, such as pre-eclampsia, intrauterine growth retardation and premature labour. Regular monitoring of hormone levels can help identify women at risk of complications and take steps to prevent or manage them.

It is therefore important that women with gestational diabetes receive regular monitoring, including appropriate hormone tests, to ensure optimal management of their condition during pregnancy **(Berdah, 2010).**

Experimental part

Material and methodes

1. Study type

We conducted a cross-sectional study. The parameters analyzed are :
Blood sugar levels, Thyroid-stimulating Hormone (TSH), Prolactin, C-peptide, Insulin, OGTT, HbA1c

2. Study population

In May 2024, blood collection tubes weregathered in Tebessa region (EHS Khaldi Abdelaziz-tebessa- and Tidjni hadem –bir el ater-) through donations from pregnant women, both diabetic and non-diabetic and non-pregnant thealthy women. These samples were submitted to Bekaria, the head of the laboratory service at the emergency medical department of the Public Hospital Establishment (EPH) Bougerra-Boulaares in the commune of bekaria, for a comprehensive hormonal profile analysis. The samples were dispatched to various locations, to obtain a hormonal profile, and also the Public Hospital Establishment Tidjanni Hadam in Bir el Ater, special thanks to the doctors in gynecology department for the help and for giving us the informations we needed to obtain an ideal result.

The Hormonal profile contains important parameters for understanding the signficance of hormonal balance in cases of gestationaldiabetes.

3. Blood sampling

Blood sampling by venipuncture is part of the pre-analytic phase which involves taking a biological sample from a human being, collecting the relevant clinical elements, preparation, and transport to the laboratory.

The following elements must be present on the sample: patient’s first and last name, age, sample number, and pathology.

4. Material

a) **Biological Material :**

The patient's blood was collected in EDTA, citrate, and Heparin tubes.

b) **Non-biological Material**

Centrifuge : to centrifugesamples

Bain-Marie: A Bain Marie at 37°C must also be used to keep the samples at constant and moderate temperature

Micropipettes: For withdrawing and transferring very small volumes of liquid with high precision (plasma or reagent)

Spectrophotometer: to measure the absorbance of a solution and determine the concentration

Printer: used to print the result obtained by the spectrophotometer

Automated immunoassay MINI VIDAS: an automated quantitative enzyme-linked fluorescent immunoassay (ELFA), for the determination of human thyroid stimulating hormone (TSH) concentration in human serum or plasma, it is intended for use as an aid in the diagnosis of thyroid or pituitary disorders.

Chemiluminescence immunoassay(CLIA): an analysis technique using artificial antigens to determine hormone concentration in blood, urine, or biological fluids.

Cobas 6000analyzer (ECLIA): is a fully automated analyzer that uses patented electrochemilumines technology for immunoassay analysis, Heterogeneous immunoassays, including cardiac markers, hormones, and infectious diseases.

Cobas e411 analyzer: The Cobas e411 analyzer is a fully automated analyzer that uses a pantentedElectroChemiLuminescence (ECL) technology for immunoassay analysis. It is designed for both quantitative and qualitative in vitro assay determinations for a broad range of applications including anemia, bone, cardiac, and tumor markers, hormones, and infectious diseases.

High-Performance Liquid Chromatography: is a technique in analytical chemistry used to separate, identify, and quantify specific components in mixtures.

5. Analysis Methods

5.1. Blood sugar levels

Glycemia is measured by venous blood sampling (where there is a sampling vein)

The patient must have been fasting for the last 8 to 12 hours at least.

The sample is in a tube using the serum obtained after centrifugation of whole blood.

Equipment used :

-Reagent, Micropipettes, Tubes, Spectrophotometer, Bain-Marie, Distilled water.

Procedure :

-First tube: Blank + reagent

-Second tube : 1000µl of reagent + 10µl of blood serum.

-Place tubes in a bain marie for 5 to 10 min.

-Set spectrophotometer « Glu » mode.

- Calibrate the spectrophotometer with the blank solution.

-Read the absorbance of the second test tube (sample)

-And finally note the indicated concentration value.

5.2. TSH (Thyroid-Stimulating-Hormone) test

Thyroid hormone levels are determined by a simple blood test, which can be formed by the time of day, To find out how well your thyroid is working and measure the amount of thyroid-stimulating hormone (TSH) in the blood, the serum blood and the reagent are placed in the automated immunoassay « Mini Vidas », Reagent for the assay are located in the sealed Reagent Strips.

Procedure :

200µl of blood serum (sample) is transferred into the well-containing anti-TSH antibody conjugated with alkaline phosphatase. The sample /conjugate mixture is cycled in and out of the SRP and TSH will bind to antibodies coated on the SRP and to the conjugate forming a « sandwich ». When completed, a report is printed for each sample.

5.3. Oral Glucose Tolerance Test

This screening isused to control the bloodsugarlevel, of the pregnantwoman to ensureitis normal. This test consists of severalbloodsamples, first on an emptystomach,

thenafter the absorption of a certain quantity of glucose, and itisperformed by taking a bloodsample in a medicalanalysislaboratoryafterfasting for 10 to 12 hours

A solution of 75g glucose concentration isprepared(Anhydre de glucose) and taken by the patient

Twobloodsamples are takenafterconsumming the solution (After 30min and one hour)

-Eachbloodsampleisanalyzed to measurebloodsugarlevels

-The average of the 2 measurementsis the absolute value of OGTT

NORMAL VALUE IS <1.50

5.4. Prolactin test

Prolactinis a hormone secreted by the pituitary gland. Although it is also part of the stress hormone circuit, its main roleis to stimulatebreastdevelopmentduringpregnancy and lactation afterchildbirth. It isadvisableto carry it out in the morning,atrest, preferably on an emptystomach, avoidingstressful situations whichcouldincreaseprolactinlevels .

Equipment :

-Chemiluminescenceimmunoassay(CLIA) on MAGLUMI 2000+

-Reagent (Anti-prolactinantibodies / enzyme-antibodyconjugate)

Procedure :

Blood iscollected in a tube for separation of serum by centrifugation

Incubation of bloodserumwithreagents for a specificperiod to allowbinding of prolactin to specificantibodies.

After incubation, the reaction mixture is washed to remove unbound substances.

The chemiluminescent reaction occurs when anti-bodies-bound prolactin reacts with chemiluminescent substances. This reaction produces light, the intensity of which is proportional to the quantity of prolactin present in the sample.

5.5. HbA1c Test :

It is a common method for measuring glucose levels on hemoglobin in red blood cells by high-performance liquid chromatography

Procedure :

-EDTA anticoagulated blood samples are collected from the patient

- After the separation of hemoglobin, it is injected into a liquid chromatograph where the different fractions are first separated according to their physical-chemical properties, Fractions are detected using an appropriate detector.

The quantity is determined compared with the total quantity of Hb and the value is expressed as a percentage or by mmol/mol.

5.6. C-peptide Test :

This test measures the level of C-peptide in a sample of your blood, Measuring C-peptide is an accurate way to find out how much insulin your body is making. It can provide important information to help understand, monitor, and/or treat disorders that involve how well your body makes insulin, such as hypoglycemia (low blood sugar) and diabetes.

The blood sample was collected into a test tube and analyzed with the Cobas e411 analyzer (ECL), For a C-peptide test you need to fast for 8 to 12 hours before the test.

-A high level of C-peptide usually means that your body ismakingtoomuchinsulin.

-A low level of C-peptide usually means the body is not making enough insulin.

5.7. Insulin test :

An insulin test is a test that measures the level of insulin in the blood, A healthcare professional will take a blood sample from a vein, using a small needle. After the needle is inserted a small amount of blood will be collected into a test tube or vial. The patient should fast for 8 to 12 hours before the test

Procedure :

Place the reagent Electrochimiluminescence on Cobas e-Roche 6000 « ECLIA », and add the blood serum to the reagent, We choose the test, identify the samples, and after starting up we wait for approximately 20min to get the results.

6. Statistical analyzes :

The normality test has been conducted. A one-way analysis of variance ANOVA was accomplished on all of the data. A post-Hoc test was excuted according to Tukey, using Prism, which allows for multiple comparaison between study groups. The results are represented in the form : mean standard deviation and differences were considered as following :

- P>0.05) the difference is not significant.
- (0.05>P>0.01) The difference is significant (*).
- (0.01>P>0.001) the difference is highly significant (**).
- (P<0.001) the difference is very highly significant (***).

We used GraphPad Prism to represent these results in the form of histogramme.

Results

The results obtained were based on three categories (Non-pregnant healthy women, healthy pregnant women, and women with gestational diabetes), The parameters measured included Glycemia, OGTT, HbA1c, insulin, c-peptide, TSH, and prolactin.

I. Biochemical parameters

1. Glycemia

According to our statistical studies, it is noticed that a very highly significant difference (P<0.001) between gestational diabetes patients compared to non-pregnant women, and pregnant women.

Table01: Glycemia level variations in non-pregnant women, pregnant women, and women with gestational diabetes.

	Glycemia (g/l)			
	Mean ± SD	CI 95%	F	P
Non-pregnant women	0.796 ± 0.0872	(0.764-0.829)		
Pregnant women	0.718 ± 0.0857	(0.686-0.750)	38.4	<.001
Gestational diabitics	0.8 ± 0.266	(0.982-1.18)		

The values are expressed as mean SD, N. Used in this analysis one-way ANOVA test supplemented by Tukey's test to classify and compare means pairwise. (P>0.05) the difference is not significant. (0.05>P>0.01) The difference is significant (*).(0.01>P>0.001) the difference is highly significant (**). (P<0.001) the difference is very highly significant(***).

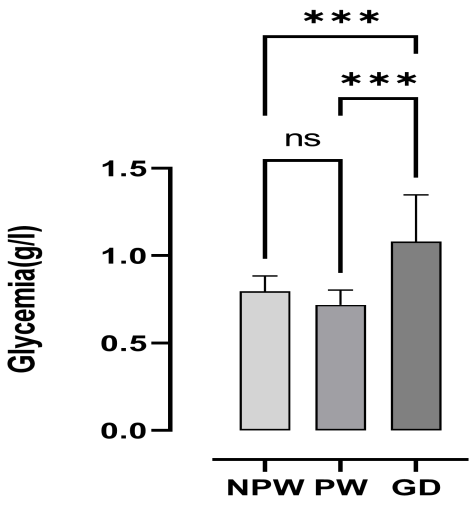

Figure 07: Glycemia (g/L) levels variations in NPW, PW and GD.

2. Oral Glucose Tolerance Test

Based on our statistical analysis, it has been observed that a very highly significant difference (P<0.001) between gestational diabetes patients compared to non-pregnant women, and pregnant women.

Table 02: OGTT level variations in non-pregnant women, pregnant women, and women with gestational diabetes.

	OGTT (g/l)			
	Mean ± SD	CI 95%	F	P
Non-pregnant women	1.00 ± 0.177	(0.956-1.04)	112	<.001
Pregnant women	1.06 ± 0.105	(1.02-1.10)		
Gestational diabitics	1.89 ± 0.416	(1.73-2.05)		

The values are expressed as mean SD, N. Used in this analysis one-way ANOVA test supplemented by Tukey's test to classify and compare means pairwise. (P>0.05) the difference is not significant. (0.05>P>0.01) The difference is significant (*).(0.01>P>0.001) the difference is highly significant (**). (P<0.001) the difference is very highly significant(***).

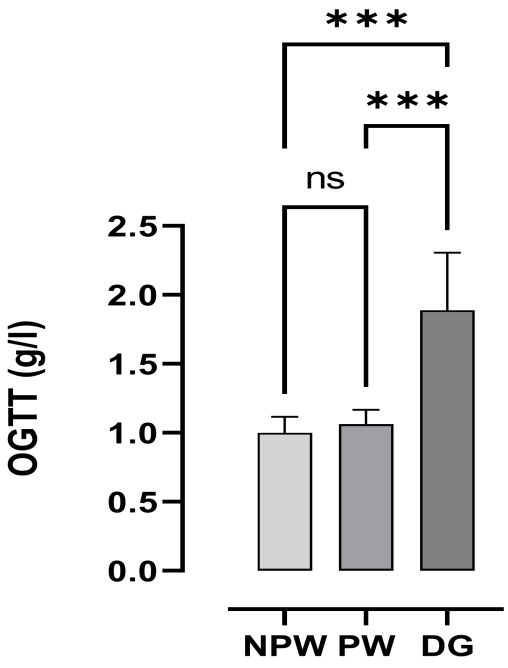

Figure08: OGTT (g/L) levels variations in NPW, PW and GD.

3. HbA1c

Through our statistical study, we noticed that there is a very highly significant difference (P<0.001) between gestational diabetes patients compared to non-pregnant women, and pregnant women.

Table 03: HbA1c level variations in non-pregnant women, pregnant women, and women with gestational diabetes.

	HbA1c(%)			
	Mean ± SD	CI 95%	F	P
Non-pregnant women	5.14 ± 0.572	(4.92-5.35)		
Pregnant women	4.96 ± 0.563	(4.76-5.17)	97.6	<.001
Gestational diabitics	7.45 ± 1.08	(7.05-7.86)		

The values are expressed as mean SD, N. Used in this analysis one-way ANOVA test supplemented by Tukey's test to classify and compare means pairwise. (P>0.05) the difference is not significant. (0.05>P>0.01) The difference is significant (*).(0.01>P>0.001) the difference is highly significant (**). (P<0.001) the difference is very highly significant(***).

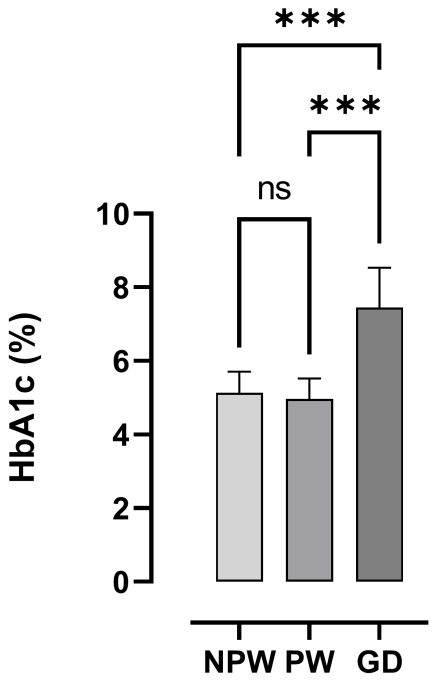

Figure09: HbA1c (%) levels variations in NPW, PW and GD.

4. Insulin

According to our statistical studies, it is noticed that a very highly significant difference (P<0.001) between gestational diabetes patients and pregnant women, and a very highly significant difference (P<0.001) between pregnant women, and non-pregnant women.

Table 04: Insulin level variations in non-pregnant women, pregnant women, and women with gestational diabetes.

	Insulin (µU/ml)			
	Mean ± SD	CI 95%	F	P
Non-pregnant women	3.98 ± 0.874	(3.65-4.31)		
Pregnant women	6.17 ± 1.03	(5.78-6.55)	24.9	<.001
Gestational diabitics	3.14 ± 2.65	(2.15-4.13)		

The values are expressed as mean SD, N. Used in this analysis one-way ANOVA test supplemented by Tukey's test to classify and compare means pairwise. (P>0.05) the difference is not significant. (0.05>P>0.01) The difference is significant (*).(0.01>P>0.001) the difference is highly significant (**). (P<0.001) the difference is very highly significant(***).

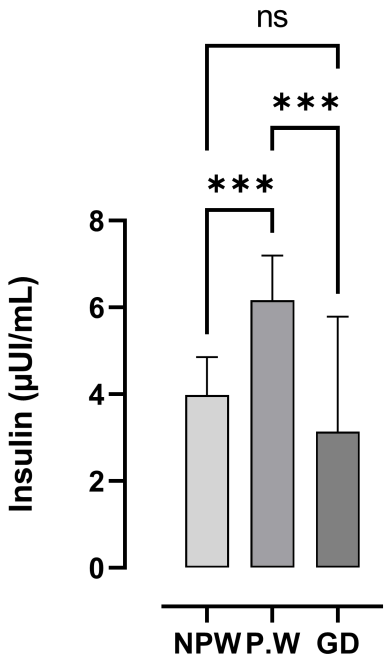

Figure10: Insulin (µUl/mL) levels variations in NPW, PW and GD .

5. C-peptide

Following our statistical study, we have concluded that there is a very highly significant difference (P<0.001) between all groups compared to each other.

Table 05: C-peptide level variations in non-pregnant women, pregnant women, and women with gestational diabetes.

C-peptide (ng/ml)				
	Mean ± SD	CI 95%	F	P
Non-pregnant women	1.63 ± 0.357	(1.49-1.76)		
Pregnant women	2.56 ± 0.435	(2.40-2.73)	63.3	<.001
Gestational diabitics	0.946 ± 0.789	(0.651-1.24)		

The values are expressed as mean SD,N. This analysis is supplemented by Tukey's test to classify and compare means pairwise.(P>0.05) the difference is not significant.(0.05>P>0.01) the difference is significant (*). (0.01>P>0.001) the difference is highly significant (**). (P<0.001) the dofference is very highly significant(***)

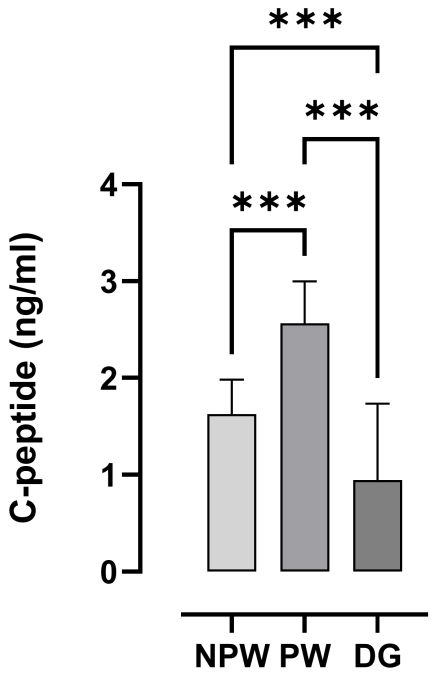

Figure11: C-peptide (ng/mL) levels variations in NPW, PW and GD.

6. TSH

The results of our statistical study concluded that a very highly significant difference (P<0.001) between gestational diabetes patients and pregnant women, a very highly significant difference (P<0.001) between gestational diabetes patients and non-pregnant women, and a significant difference (0.05>P>0.01) between pregnant women and non-pregnant women.

Table 06: TSH level variations in non-pregnant women, pregnant women, and women with gestational diabetes.

TSH (µlU/mL)				
	Mean ± SD	CI 95%	F	P
Non-pregnant women	1.85 ± 1.15	(1.42-2.28)		
Pregnant women	1.13 ± 0.718	(0.867-1.40)	87.8	<.001
Gestational diabitics	4.54 ± 1.21	(4.08-4.99)		

The values are expressed as mean SD,N. This analysis is supplemented by Tukey's test to classify and compare means pairwise.(P>0.05) the difference is not significant.(0.05>P>0.01) the difference is significant (*). (0.01>P>0.001) the difference is highly significant (**). (P<0.001) the dofference is very highly significant(***)

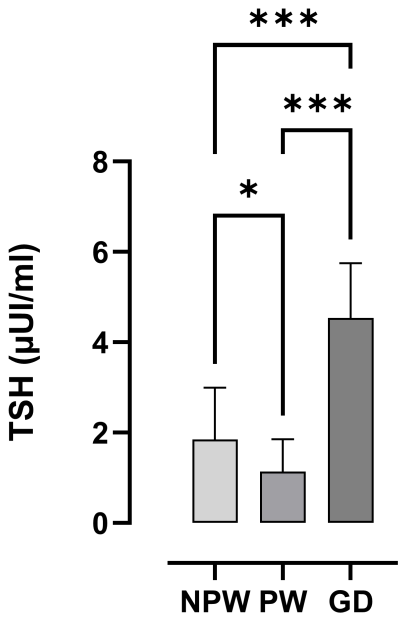

Figure12: TSH (µUI/mL) levels variations in NPW, PW and GD.

II. Immunological parameters

1. Prolactin

After our statistical study, we found that our results indicate the presence of a very highly significant difference (P<0.001) between gestational diabetes women and non-pregnant women, a significant difference (0.05>P>0.01) between gestational diabetes women and pregnant women, and a very highly significant difference (P<0.001) between non-pregnant women and pregnant women.

Table 07: prolactin level variations in non-pregnant women, pregnant women, and gestational diabetics.

Prolactin (µlU/mL)				
	Mean ± SD	CI 95%	F	P
Non-pregnant women	237 ± 96.5	(201-273)		
Pregnant women	2912 ± 1002	(2538-3286)	147	<.001
Gestational diabitics	3514 ± 925	(3169-3860)		

The values are expressed as mean SD,N. This analysis is supplemented by Tukey's test to classify and compare means pairwise.(P>0.05) the difference is not significant.(0.05>P>0.01) the difference is significant (*). (0.01>P>0.001) the difference is highly significant (**). (P<0.001) the dofference is very highly significant(***)

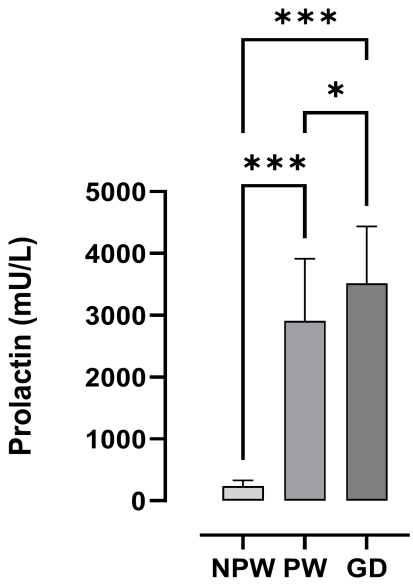

Figure13: Prolactin (mU/L) levels variations in NPW, PW and GD.

III. Correlation

Table 08: Person's correlation between hormones and gestational diabetes profile.

Pearson's R correlation							
	Glycemia	**OGTT**	**HbA1c**	**Insulin**	**C-peptide**	**TSH**	**Prolactine**
Glycemia	/	0.755***	0.826***	-0.592***	-0.619***	0.626***	0.255*
OGTT	0.755***	/	0.840***	-0.345***	-0.470***	0.692***	0.508***
HbA1c	0.826***	0.840***	/	-0.424***	-0.570***	0.755***	0.490***
Insulin	-0.592***	-0.345***	-0.424***	/	0.891***	-0.416***	0.170
C-peptide	-0.619***	-0.470***	-0.570***	0.891***	/	-0.602***	0.00635
TSH	0.626***	0.692***	0.755***	-0.416***	-0.602***	/	0.426***
Prolactine	0.255*	0.508***	0.490***	0.170	0.00635	0.426***	/

OGTT; Oral Glucose Tolerance Test, HbA1c;Hemoglobin type A separated on cation exchange chromatography,C-peptide; connecting peptide, TSH; Thyroid-stimulation Hormone, /; not established, *: (P<0.05), **: (P>0.01), ***: (P<0.001

Discussion

Gestational diabetes, defined as diabetes first diagnosed in the second or third trimester of pregnancy, is a common metabolic disorder in pregnant women. This investigation aims to study the following biochemical and immunological parameters (Glycemia, OGTT, HbA1c, c-peptide, insulin, TSH, and Prolactin) and their variation in the three populations: (Non-pregnant healthy women, Pregnant Healthy women, and women with gestational diabetes)
Based on the various statistical tools used on the studied population, we were able to highlight several observations:

C-peptide is a small molecule produced when proinsulin is split into insulin in the beta cells of the pancreas. It is released at the same time as insulin into the bloodstream. C-peptide is considered to be an indirect marker of endogenous insulin production in the pancreas.

Our research identified a positive association between early-pregnancy serum C-peptide levels and the risk of developing GD. A high level of C-peptide generally indicates a high level of endogenous insulin production. This may be in response to a high blood glucose caused by glucose intake and/or insulin resistance. This relationship was also evident through significant correlations between C-peptide and other metabolic biomarkers in pregnant women. These findings suggest that C-peptide levels in early pregnancy may serve as an important risk factor for GD and could potentially predict the condition. **(Milionis *et al.*, 2024)**

Thyroid hormones significantly affect glucose metabolism and insulin sensitivity. Consequently, abnormal tsh level in the GD group which indicates a thyroid function disorder, impacts glucose metabolism and C-peptide secretion.

There appears to be an interesting observation that thyroid-stimulating hormone (TSH) levels were higher in the gestational diabetes (GD) group compared with the other groups, while TSH levels were lower in the non-diabetic pregnant group (gestational group). This observation raises several points for consideration:

Relationship between thyroid and gestational diabetes: our research has suggested a link between thyroid function and gestational diabetes. Impaired thyroid function, including elevated TSH levels or hypothyroidism, has been associated with an increased risk of gestational diabetes.Forthermore, in GD fasting glycemia,OGTT and HbA1c were higher in the GD group (**Ying *et al.*, 2016)**

Discussion

Prolactin, a hormone produced by the anterior pituitary gland, may influence glucose metabolism and have implications for HbA1c and OGTT results. Studies have suggested that prolactin may influence glucose regulation in the body. High levels of prolactin may be associated with impaired glucose tolerance and an increased risk of diabetes.

If prolactin influences glucose regulation, high prolactin levels could potentially affect HbA1c results by increasing blood glucose levels and thus raising HbA1c levels. Also affect OGTT results by altering the body's response to administered glucose **(Rassie *et al* ., 2022)**

Conclusion

Through this study and the analyses we obtained, we found that gestational diabetes is quite common in Tebessa. GD is a major cause of pregnancies at risk of maternal-fetal complications. For prevention to be effective, screening must be sufficiently early and systematized by means of an orally induced hyperglycemia test. Standardized follow-up by a multidisciplinary team (gynecologist-obstetrician, internist, nutritionist, midwife and neonatalogist) is essential. It is also important to make pregnant women aware of the need for post-partum metabolic monitoring, as these women are at increased risk of subsequent hyperglycemia.

Finally, these tests are performed to obtain sufficient results to understand the importance of this assessment in the case of gestational diabetes, and help monitor glucose regulation during pregnancy and adjust treatment if necessary to prevent complications for mother and baby.

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Web sites

FRED
https://diabete-enfants.ca/

Soufianeadjana 2022
https://www.sfdiabete.org/medical/evenements/congres-sfd/congres-sfd-2022

Appendix

	Résultats	Unités	Valeurs Usuelles	Antécédants
HORMONOLOGIE				
Insuline *"ECLIA" électrochimiluminescence sur Cobas e - Roche sur Cobas 6000*	4.71	µUI/mL	2.6 - 24.9	
Peptide C *Electrochimiluminescence (ECL) - sur Cobas e411*	1.99 0.66	ng/ml nmol/L	0.30 - 10.0 0.09 - 3.33	
Prolactine *Chimiluminescence (CLIA) - sur MAGLUMI 2000+(2)*	97.12 * 2068.66	ng/mL mUI/L	3.10 - 23.03 66.03 - 490.53	

Résultat validé par : Dr BELLIL.T

Ouvert du Samedi au Jeudi de 7:30 a 16:30

RESULTATS DES ANALYSES MEDICALES

Examen demandé	Résultat	UNIT	Valeur de réf
HbA1c, hémoglobine glyquée HPLC (chromatographie liquide) - Tosoh GX	5.2	%	4.4--------6.2 non diabetique > 6.2 diabetique 6.5--------8.2 diabetique bon controle >8.2 diabetique mauvais controle
HbA1c (IFCC)	37.6	mmol/moL	24 --- 44.3

BEKKARIA LE: 04.05.2024

PHARMACIE BISKRI.S
R.C.N° 02 A 2911391
Tel : 037 51 85 ...
Bekkaria W.Tébessa

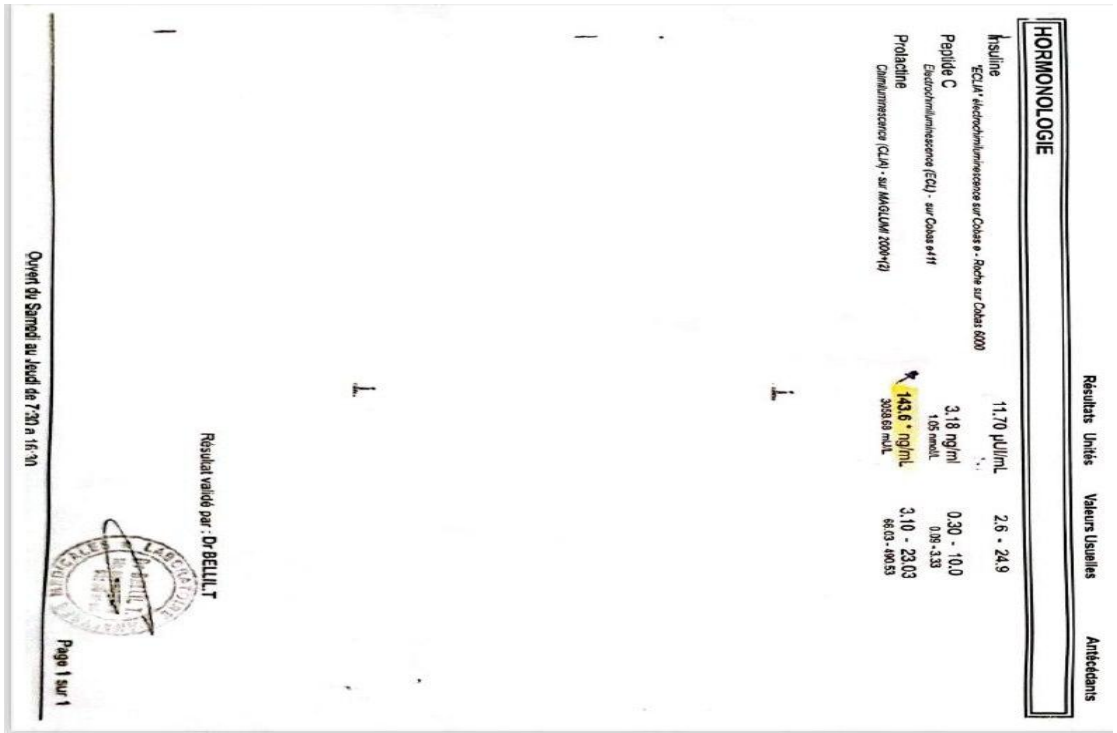
LE PHARMACIEN

Appendix

	Résultat	Normes
BIOCHIMIE		
Gly	* 0.50 g/l	0.70 - 1.10
THYROIDE		
TSH	1.28 µUI/ml	0.38 - 4.31

ZOGHLAMI Tidjani
Biologiste Principal

المؤسسة العمومية الاستشفائية
بوقرة بولعراس – قيمة
التخبير المركزي – الكيمياء الحيوية



HORMONOLOGIE

	Résultats	Unités	Valeurs Usuelles	Antécédents
Insuline *ECLIA électrochimiluminescence sur Cobas s - Roche sur Cobas 6000*	11.70	µU/mL	2.6 - 24.9	
Peptide C *Electrochimiluminescence (ECL) - sur Cobas e411*	3.18 1.05	ng/ml nmol/L	0.30 - 10.0 0.09 - 3.33	
Prolactine *Chimiluminescence (CLIA) - sur MAGLUMI 2000+(2)*	143.6 * 3059.69	ng/mL mUI/L	3.10 - 23.03 66.03 - 490.53	

Ouvert du Samedi au Jeudi de 7:30 a 16:30

Résultat validé par : Dr BELILI.T

Page 1 sur 1

Appendix

RESULTATS DES ANALYSES MEDICALES

Examen demandé	Résultat	UNIT	Valeur de réf
HbA1c, hémoglobine glyquée HPLC (chromatographie liquide) - Tosoh GX	6.8	%	4.4---------6.2 non diabetique > 6.2 diabetique 6.5---------8.2 diabetique bon controle >8.2 diabetique mauvais controle
HbA1c (IFCC)	46.22	mmol/moL	24 - - -- 44.3

BEKKARIA LE: 04.05.2024

LE PHARMACIEN

PHARMACIE BASKRI
Tel : 037 52 85 [illegible]
Bekkaria W.Tébessa

	Résultat	Normes
BIOCHIMIE		
Gly	*0.55 g/l	0.70 - 1.10
THYROIDE		
TSH	1.05 µUI/ml	0.38 - 4.31

ZOGHLAMI Tidjani
Biologiste Principal

	Résultats	Unités	Valeurs Usuelles	Antécédants
HORMONOLOGIE				
Insuline *"ECLIA" électrochimiluminescence sur Cobas e - Roche sur Cobas 6000*	1.59	µUI/mL	2.6 - 24.9	
Peptide C *Electrochimiluminescence (ECL) - sur Cobas e411*	1.59 0.52	ng/ml nmol/L	0.30 - 10.0 0.09 - 3.33	
Prolactine *Chimiluminescence (CLIA) - sur MAGLUMI 2000+(2)*	>235 *	ng/mL	3.10 - 23.03	

Résultat validé par : Dr BELLIL.T

Ouvert du Samedi au Jeudi de 7:30 a 16:30

	Résultat	Normes
BIOCHIMIE		
Gly	*0.60 g/l	0.70 - 1.10
THYROIDE		
TSH	2.31 µUI/ml	0.38 - 4.31

ZOGHLAMI Tidjani
Biologiste Principal

المؤسسة العمومية الاستشفائية
بوقرة بولعراس – تبسة
المخبر المركزي – الكيمياء الحيوية

RESULTATS DES ANALYSES MEDICALES

Examen demandé	Résultat	UNIT	Valeur de réf
HbA1c, hémoglobine glyquée HPLC (chromatographie liquide) - Tosoh GX	6.9	%	4.4---------6.2 non diabetique > 6.2 diabetique 6.5---------8.2 diabetique bon controle >8.2 diabetique mauvais controle
HbA1c (IFCC)	46.8	mmol/moL	24 - - - 44.3

BEKKARIA LE: 04.05.2024

LE PHARMACIEN

PHARMACIE BISKRI
Bekkaria W.Tébessa

CONTRÔLE DE QUALITE

- REF 95010 EXATROL-N Taux I
- REF 95011 EXATROL-P Taux II
- REF 95012 Contrôles urinaires (Taux 1 et Taux 2)
- Programme externe de contrôle de la qualité

Il est recommandé de contrôler dans les cas suivants :

- Au moins un contrôle par série
- Au moins un contrôle par 24 heures
- Changement de flacon de réactif
- Après opérations de maintenance sur l'analyseur

Lorsqu'une valeur de contrôle se trouve en dehors des limites, appliquer les actions suivantes :

1. Préparer un contrôle frais et répéter le test.
2. Si la valeur obtenue reste en dehors des limites, utiliser un calibrateur frais.
3. Si la valeur obtenue reste en dehors des limites, répéter le test en utilisant un autre flacon de réactif.

Si la valeur obtenue reste en dehors des limites, contacter le service technique BIOLABO ou le revendeur local.

INTERVALLES DE REFERENCE (1)

Dans le sérum ou le plasma :	g/L	(mmol/L)
Nouveau-né, 1 jour	0,40-0,60	[2,2-3,3]
Nouveau-né > 1 jour	0,50-0,80	[2,8-4,4]
Enfant	0,60-1,00	[3,3-5,6]
Adulte	0,74-1,06	[4,1-5,9]
60-90 ans	0,82-1,15	[4,6-6,4]
> 90 ans	0,75-1,21	[4,2-6,7]

Dans le LCR	g/L	(mmol/L)
Enfant	0,60-0,90	[3,3-4,4]
Adulte	0,40-0,70	[2,2-3,9]

Dans les urines de 24 h	0,01 à 0,15 g/L (0,1-0,8 mmol/L)
	<0,5 g/24 h (<2,78 mmol/24 h)

Il est recommandé à chaque laboratoire de définir ses propres valeurs de référence pour la population concernée.

PERFORMANCES

Sur Konza 240TX, 37°C, 505 nm

Limite de détection : environ 0,1 g/L

Précision :

Intra-série N = 20	Taux bas	Taux moyen	Taux élevé	Inter-série N = 20	Taux bas	Taux moyen	Taux élevé
Moyenne (g/L)	0,35	1,38	2,22	Moyenne (g/L)	0,37	1,15	2,32
S.D. g/L	0,01	0,02	0,02	S.D g/L	0,016	0,047	0,097
C.V. %	2,9	1,5	0,9	C.V. %	4,7	4,1	4,2

Domaine de mesure :

entre 0,25 g/L (1,39 mmol/L) et 5,00 g/L (28 mmol/L)

Sensibilité analytique : (méthode manuelle) :

0,420 abs pour 1 g/L (505 nm, 1 cm de trajet optique)

Comparaison avec réactif du commerce :

Avec n= 61 spécimens entre 0,24 et 3,57 g/L

y = 0,969 – 0,0133 r = 0,9984

Interférences :

Acide ascorbique	Interférence négative à partir de 100 mg/L
Bilirubine totale	Interférence négative à partir de 275 µmol/L
Hémoglobine	Pas d'interférence jusqu'à 434 µmol/L
Turbidité	Interférence positive à partir de 0,100 abs.

D'autres substances sont susceptibles d'interférer (voir § Limites)

CALIBRATION (6)

- REF 95015 Multicalibrator traçable sur SRM 965b
- Etalon (flacon R3) : Méthode manuelle et usines.

La fréquence de calibration dépend des performances de l'analyseur et des conditions de conservation du réactif.

Effectuer une nouvelle calibration en cas de changement de lot de réactif, si les résultats des contrôles sont hors de l'intervalle établi, et après opération de maintenance.

PROCEDURE

Méthode manuelle

Ramener les réactifs et échantillons à température ambiante.

Réactif	1000 µL
Blanc, Calibrateur, Contrôle ou spécimen (1)	10 µL

Bien mélanger. Incuber 10 minutes à 37°C ou 20 minutes à température ambiante. Lire les absorbances à 505 nm (460-560) contre le blanc réactif.

La coloration est stable 15-20 minutes à 37°C, puis décroît lentement.

Remarques :

1. Sérum, plasma ou urines diluées dans NaCl 9 g/L.
2. Les performances en technique manuelle doivent être établies par l'utilisateur.
3. Les applications Konza et d'autres propositions d'applications sont disponibles sur demande.

CALCUL

Sérum ou plasma

$$\text{Résultat} = \frac{\text{Abs (Dosage)}}{\text{Abs (Calibrateur)}} \times \text{concentration du Calibrateur}$$

Urines : Multiplier par le facteur de dilution approprié

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(6) BERNARD J., Biochimie clinique, 2ème ed. Expansion Scientifique Paris (1998), p. 165-167
(7) SRM : Standard Reference Material ®

Appendix

BIOLABO
www.biolabo.fr
FABRICANT :
BIOLABO SAS,
Les Hautes Rives
02160, Maizy, France

GLUCOSE GOD-PAP

Réactif pour le dosage quantitatif du glucose dans le sérum et le plasma humains, les urines ou le liquide céphalorachidien (LCR)

REF 87409	R1	10 x 100 mL	R2	10 x 100 mL	R3	1 x 5 mL

SUPPORT TECHNIQUE ET COMMANDES
Tel : (33) 03 23 25 15 50
support@biolabo.fr
Dernière révision : www.biolabo.fr

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I correspond aux modifications significatives

I USAGE PREVU

Ce réactif est réservé pour un usage professionnel en laboratoire (méthode manuelle ou automatisée).
Il permet de mesurer la quantité de glucose dans le plasma, le sérum et le liquide céphalorachidien (LCR) humains, ou les urines pour en évaluer le taux.

GENERALITES (1) (6)

La concentration en glucose sanguin est maintenue à l'intérieur de limites relativement etroites dans différentes situations (absorption de nourriture, jeûne ou exercice intense) par des hormones régulatrices comme l'insuline, le glucagon ou l'épinéphrine. Le dosage du glucose est un des tests les plus fréquemment réalisés au laboratoire d'analyses médicales, conjointement avec d'autres tests de tolérance (épreuve d'hyperglycémie provoquée, glycémie post-prandiale...).
Le désordre du métabolisme des carbohydrates sanguins le plus couramment rencontré est l'hyperglycémie due au diabète mellitus.

Une hyperglycémie supérieure à 3,0 g/L (16,5 mmol/L) peut conduire à une céto-acidose et un coma hyperosmolaire.

Toute hypoglycémie durable, inférieure à 0,30 g/L (1,7 mmol/L), est susceptible d'entraîner des lésions encéphaliques graves et irréversibles.

PRINCIPE (4) (5)

Méthode de Trinder.
Le glucose est oxydé par la GOD en acide gluconique et H_2O_2 qui réagit en présence de POD avec le chloro-4-phénol et le PAP pour former une quinonéimine rouge. L'absorbance du complexe coloré, proportionnelle à la concentration en glucose dans le spécimen est mesurée à 500 nm.

REACTIFS

R1	**GLUCOSE GOD PAP**	Tampon-Enzymes
Tampon phosphate	150	mmol/L
Glucose oxydase (GOD)	≥ 20 000	UI/L
Péroxydase (POD)	≥ 1000	UI/L
4-Amino-antipyrine (PAP)	0,8	mmol/L
R2	**GLUCOSE GOD PAP**	Chromogène
Chloro-4-phénol	2	mmol/L
R3	**GLUCOSE GOD PAP**	Etalon
Glucose	1	g/L (5,55 mmol/L)

Ces réactifs ne sont pas classés comme dangereux selon le règlement 1272/2008/CE

PRECAUTIONS

- Consulter la FDS en vigueur disponible sur demande ou sur www.biolabo.fr
- Vérifier l'intégrité des réactifs avant leur utilisation.
- Elimination des déchets : respecter la législation en vigueur.
- Traiter tout spécimen ou réactif d'origine biologique comme potentiellement infectieux. Respecter la législation en vigueur.

I Tout incident grave survenu en lien avec le dispositif fait l'objet d'une notification au fabricant et à l'autorité compétente de l'État membre dans lequel l'utilisateur et/ou le patient est établi.

PREPARATION DES REACTIFS

Utiliser un objet non coupant pour enlever la capsule.
Verser sans délai le contenu du flacon R1 dans le flacon R2.
Mélanger doucement jusqu'à dissolution.
Flacon R3 : Prêt à l'emploi

STABILITE ET CONSERVATION

Stockés à l'abri de la lumière, dans le flacon d'origine bien bouché à 2-8°C, les réactifs sont stables, s'ils sont utilisés et conservés dans les conditions préconisées :
Avant ouverture :
- Jusqu'à la date de péremption indiquée.

Après ouverture :
- Reconstituer le réactif R1 immédiatement après ouverture.
- Etalon : Transférer la quantité utile et remettre le flacon à 2-8°C.

Après reconstitution :
- Transférer la quantité utile et stocker le flacon à 2-8°C.
- Le réactif de travail est stable 2 ans.
- Rejeter tout réactif trouble ou si le blanc réactif à 500 nm > 0,400.
- Ne pas utiliser le réactif de travail après la date de péremption.

PRELEVEMENT ET PREPARATION DU SPECIMEN (2)

Sérum ou plasma
Séparé rapidement des cellules sanguines pour prévenir la glycolyse. Si le fluorure est utilisé comme conservateur, une diminution de 0,09 g/L (0,5 mmol/L) est observée dans les deux premières heures, la concentration se stabilise ensuite.

Le glucose est stable dans le sérum et le plasma hépariné :
- 8 h à 25°C ou 72 h à 2-8°C.

Le glucose est stable dans le plasma (fluorure de sodium ou iodoacétate) :
- 24 h à température ambiante.

LCR : Analysé immédiatement après collecte pour éviter des résultats sous évalués. Conserver à –20°C.

Urines : collectées en flacon opaque et conservées à 2-8°C. Conserver les urines de 24 h avec 5 mL d'acide acétique glacial ou 5 g de sodium benzoate ou fluorure.

LIMITES (3)

Young D.S. a publié une liste des substances interférant avec le dosage.

REACTIFS ET MATERIEL COMPLEMENTAIRES

1 Equipement de base du laboratoire d'analyses médicales.
Spectrophotomètre ou Automate de biochimie

Appendix

Bain-Marie

Centrifuge

Spectrophotometer

TSH reagent

TSH reagent

Glycemia reagent

Immunoassay Analyzer MINI VIDAS

CLIA maglumi 2000 Plus

Cobas e411 (ECL)

Automated Analyzer Roche Cobas 6000 (ECLIA)	Micropipette