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FMU-9997

Addressograph

-INFORMATION and CONSENT DOCUMENT-

STUDY TITLE: Determining prevalence and predictors of non-alcoholic fatty liver disease in patients with polycystic ovary syndrome: The **F**atty **LI**ver in **P**olycystic **O**vary **S**yndrome (**FLIPCOS**) study

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INTRODUCTION

You are being invited to take part in this study because you have PCOS and might have liver disease called NAFLD.

Before deciding to participate in this research study, you should understand the content of this consent form, the risks and benefits to make an informed decision, and ask questions if there is anything you do not understand. Please read this entire consent form which contains a full explanation of the study and take your time to take a decision. If you decide to participate in this research study you will be asked to sign and date this form, and a copy will be given to you. Feel free to ask any questions at any time throughout the study.

BACKGROUND

Non-alcoholic fatty liver disease (NAFLD) is a metabolic liver disease caused by the build-up of fat within the liver. If left untreated, it might progress to non-alcoholic steatohepatitis (NASH) which is an inflammatory condition that can lead to liver cirrhosis, a serious condition characterized by scarring liver tissue that prevents the liver from functioning normally. NAFLD has been strongly associated with PCOS and metabolic syndrome which consists of diabetes and high sugar levels in the blood, central obesity, high cholesterol and hypertension. Insulin resistance and hyperandrogenesim that are the predominant metabolic abnormalities in polycystic ovary syndrome play a cardinal role in developing NAFLD in these patients. Many studies worldwide came with the conclusion that NAFLD is not an uncommon condition in PCOS cases. However, none of these studies have used a diagnostic tool, which is accurate as the liver biopsy. Formerly, liver biopsy was long been the only reliable way and the gold standard procedure to diagnose NAFLD and NASH. Nevertheless, its invasiveness has created a deficiency in the scientific information. Carrying out this research study with a non-invasive diagnostic procedure that is resembling the ultrasound and is reliable as the biopsy, might uncover the exact prevalence of NAFLD as well as the predictors of the disease in the Canadian society. It will subsequently increase the clinician's awareness about the emerging burden of this medical issue.

PURPOSE OF THE STUDY

To estimate the prevalence of NAFLD and its predictors using non-invasive diagnostic tests (Fibroscan); an easy, painless, and reliable bedside procedure to diagnose NAFLD in PCOS.

STUDY DESCRIPTION

You will be asked to come to the study site for a visit: During this visit you will be asked to fill up questionnaires, you will undergo a thorough medical examination, a blood tests will be drawn and ultrasonographic studies (if applicable) and Fibroscan will be performed.

STUDY DESCRIPTION AND PROCEDURES

If you agreed to take part in this study and you are already holding the diagnosis of PCOS, you will undergo only tests that are required to exclude conditions that might contribute to liver disease and the Fibroscan to determine the presence of fatty liver. However, if you are suspected to have PCOS and not yet confirmed, we will confirm that you meet the medical criteria for PCOS diagnosis by performing the tests listed below. We will also confirm that you do not have any other illnesses that

can contribute to liver disease. If after these tests you are found to be eligible to participate in the study, you will undergo Fibroscan.

Study Visit for patients who have not been confirmed to have PCOS (1 ½ hours):

- Questionnaire: You will be asked to fill up a questionnaire. Your demographic characteristics, smoking habits, alcohol use, diet and exercise will be reviewed.
- Physical exam: You will have a complete clinical examination, including measurement of your vital signs, checking your heart, lungs, examination of your abdomen and of the liver.
- Review of medical history: Your current medication, current medical history, Hepatitis B, C, and HIV status will be reviewed and recorded.
- Medical chart review: Your medical chart will be reviewed for your medication and medical history.
- Blood tests: Routine blood tests as per standard of care will be drawn (about 7 mL – 1 ½ teaspoons) including CBC with differential, Biochemistry, hepatic function, lipid profile, ANA, glucose, hemoglobin glycosylated, fasting serum insulin. Hormonal studies will be done such as serum testosterone, FAI, dehdroepiandrosterone sulfate, Estradiol, LH, FSH, TSH, and PRL.
- Hepatitis B, C, and HIV status will be confirmed: if your status is not known for more than 2 years, these tests will be repeated. Confirmation of Hepatitis B, C and HIV status is being done to exclude any other potential liver diseases that might affect the measurement of the desired outcome. If you are found positive for any of these, you will be referred to an appropriate healthcare provider.
- Ultrasonographic study (Transvaginal U/S): This procedure is performed at the bedside in the clinic as per standard of care by inserting the ultrasound probe inside the vagina. This test is done to obtain ultrasonographic images that are used for the diagnosis PCOS.
- Pregnancy test: If you are a woman able to bear children, a pregnancy test will be performed. The test must be negative for you to take part in the study.
- Fibroscan: You will need to fast for 2-4 hours before the Fibroscan, but sips of water are acceptable. This procedure is performed at the bedside in the clinic, a mechanical pulse will be generated at the skin surface, which will spread through the liver. The speed of the wave will be measured by ultrasound. The speed of this wave is related to the stiffness of the liver, which in turn reflects the degree of liver damage – the stiffer the liver is the greater the damage to the liver.

Study Visit for patient who are already been diagnosed as PCOS (1 hour):

- Questionnaire: You will be asked some questions to fill up a questionnaire. Your smoking habits, alcohol use, diet and exercise will be reviewed.
- Physical exam: You will have a complete clinical examination, including your vital signs.
- Review of medical history: Your current medication, current medical history, Hepatitis B, C, and HIV status will be reviewed and recorded.
- Medical chart review: Your medical chart will be reviewed for your medication and medical history.
- Blood tests: Routine blood tests as per standard of care will be drawn (about 7 mL – 1 ½ teaspoons) including CBC with differential, Biochemistry, hepatic function, lipid profile, ANA, glucose, hemoglobin glycosylated, fasting serum insulin, and pregnancy test.
- Hepatitis B, C, and HIV status will be confirmed: if your status is not known for more than 2 years, these tests will be repeated. Confirmation of Hepatitis B, C and HIV status is being done to

exclude any other potential liver diseases that might affect the measurement of the desired outcome. If you are found positive for any of these, you will be referred to an appropriate healthcare provider.

- Pregnancy test: If you are a woman able to bear children, a pregnancy test will be performed. The test must be negative for you to take part in the study.
- Fibroscan: You will need to fast for 2-4 hours before the Fibroscan, but sips of water are acceptable. This procedure is performed at the bedside in the clinic, a mechanical pulse will be generated at the skin surface, which will spread through the liver. The speed of the wave will be measured by ultrasound. The speed of this wave is related to the stiffness of the liver, which in turn reflects the degree of liver damage – the stiffer the liver is the greater the damage to the liver.

POTENTIAL RISKS AND DISCOMFORTS

Blood Draw Risks

Blood drawing may cause some discomfort, bleeding or bruising where the needle enters the body (1%). A small blood clot may form at this site or there may be swelling in the area. Rarely, fainting or local infection may occur. Care will be taken to prevent these complications.

Transvaginal Ultrasound Risk

It is painless, non-invasive yet uncomfortable, and involves no exposure to radiation. There are no associated risks. This procedure may produce a minimal discomfort. Otherwise, it is considered a safe procedure.

Fibroscan Risks

No risks or contraindications relating to patient safety have been identified; however, the manufacturer recommends that the following are contraindications to Fibroscan: Pregnancy, Pacemaker or other implantable device, and ascites. In addition, there may be other risks unknown at this time.

PREGNANCY

You cannot take part in this study if you are pregnant, think that you may be pregnant, or are trying to get pregnant. You should inform your study doctor if you suspect to be or become pregnant during the study.

POTENTIAL BENEFITS

You may or may not directly benefit from your participation in this study. However, this research study is part of an effort to collect more information about non-invasive methods for treating/detecting NAFLD and NASH, which may provide potential benefit to others in the future.

REIMBURSEMENT AND COMPENSATION

You will not be reimbursed for any of the costs related to your participation in this study.

SHOULD YOU SUFFER ANY HARM

Should you suffer any kind of harm following a procedure related to the research study, you will receive

the appropriate care and services required by your state of health.

By agreeing to participate in this research project, you are not waiving any of your legal rights nor discharging the study doctor, the sponsor or the institution, of their civil and professional responsibilities.

CONFIDENTIALITY

During your participation in this study, the study doctor and their team will collect and record information about you in a study file. They will only collect information required to meet the scientific goals of the study.

The study file may include information from your medical chart, including your identity, concerning your past and present state of health, your lifestyle, as well as the results of the tests, exams, and procedures that you will undergo during this research project. Your research file could also contain other information, such as your name, sex, date of birth and ethnic origin.

The blood samples will be analyzed and destroyed after analysis. All data for the study including questionnaires, blood results, U/S and fibroscan results will be stored at the MUHC. Study data will be used for exclusive objectives described in this consent form.

All the information collected during the research project will remain strictly confidential to the extent provided by law. You will only be identified by a code number. The key to the code linking your name to your study file will be kept by the study doctor.

The study data will be stored for 7 years after study completion and then destroyed. The data may be published or shared during scientific meetings; however, it will not be possible to identify you.

For auditing purposes your study file may be examined by individuals mandated by the funder, the McGill University Health Centre, or the Research Ethics Board. All these individuals adhere to policies on confidentiality.

VOLUNTARY PARTICIPATION/WITHDRAWAL

Your participation in this study is voluntary. Therefore, you may refuse to participate. You may also withdraw from the ongoing project at any time, without giving any reason, by informing a member of the study team. Your decision not to participate in the study, or to withdraw from it, will have no impact on the quality of care and services to which you are otherwise entitled. You will be informed in a timely manner if any information becomes available that may impact your willingness to continue participating in this study.

If you withdraw or are withdrawn from the study, you may also request that the data already collected about you be removed from the study. If you request that your data be removed, and the information already collected about you can be identified as yours it will be destroyed. If the data has been anonymized or was always anonymous (e.g. does not contain any information that can be used to identify you), the data will continue to be used in the analysis of the study.

INDIVIDUAL RESEARCH RESULTS AND INCIDENTAL FINDINGS

As part of this research study, we may find that you have non-alcoholic fatty liver disease (NAFLD). If you are found to have NAFLD, this result will be communicated to you and a healthcare professional of your choice.

Material incidental findings are unexpected findings made in the course of the study that may have significant impacts on your current or future wellbeing or that of your family members. A material incidental finding concerning you in the course of this research will be communicated to you and to a health professional of your choice.

CONTROL OF THE ETHICAL RESEARCH ASPECTS OF THE RESEARCH PROJECT

The Research Ethics Board of the McGill University Health Centre approved this study and is responsible for following study and making sure that you are protected. Before any change is made to the Information and Consent Form or to the study, it must first be approved by the Research Ethics Board.

CONTACT INFORMATION

If you have questions about this clinical research study, you may contact, Dr. Giada Sebastiani during working hours at (514) 843-2090, Dr. Srinivasan Krishnamurthy during working hours at (514) 9341934, ext. 35005.

If you have questions concerning your rights as a Research Participant and wish to discuss them with someone not connected to the clinical research study, please contact the Ombudsman of the McGill University Health Centre (514) 934-1934 extension 35655.

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DECLARATION OF CONSENT

I am aware that by initialing each page of the Consent Form and signing the signature page:

- ☐ I have read the entire document and all my questions have been answered to my satisfaction. I am free to ask further questions at any time during the study, and I will receive a copy of this Consent Form for my records.
- ☐ All personal data collected will remain confidential and that any resulting publication will maintain my anonymity.
- ☐ My participation in the study is voluntary and that I am completely free to refuse to participate or to withdraw from this study at any time without this changing in any way the quality of care that I will receive.
- ☐ I am not waiving any of my legal rights nor am I freeing the investigators, sponsors or the health establishment from their legal and professional responsibilities.
- ☐ There is no guarantee that this study will provide any benefit to me.

Printed Name of Participant	Signature of Participant	Date (dd/mm/yyyy)

Printed Name of Investigator/ Delegate Obtaining Consent	Signature of Investigator/ Delegate Obtaining Consent	Date (dd/mm/yyyy)

The potential benefits, risks and procedures associated with this study have been fully explained to the volunteer and he or she has had ample time and opportunity to ask questions and to decide whether or not to participate in this study.

Name of person obtaining consent	Signature of person obtaining consent	Date (dd/mm/yyyy)