INCIDENCE OF GESTATIONAL DIABETES MELLITUS IN HIV POSITIVE ANTENATAL WOMEN ON ANTIRETROVIRAL THERAPY

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **" INCIDENCE OF GESTATIONAL DIABETES MELLITUS IN HIV POSITIVE ANTENATAL WOMEN ON ANTIRETROVIRAL THERAPY"** is a bonafide record work done by Dr. Shwetha.S under my direct supervision and guidance , submitted to Tamil Nadu Dr. M.G.R . Medical University in partial fulfillment of University regulations for MS Obstetrics and Gynaecology.

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DECLARATION

I Dr. Shwetha .S solemnly declare that the dissertation tiltled **“INCIDENCE OF GESTATIONAL DIABETES MELLITUS IN HIV POSITIVE ANTENATAL WOMEN IN ANTIRETROVIRAL THERAPY”** has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other person for any award ,degree or diploma to any other university board either in India or abroad.

This is submitted to The Tamil Nadu Dr. MGR Medical University, Chennai in partial fulfillment of the rules and regulations for the award of M.S degree Branch II Obstetrics and Gynaecology to be held in March 2016

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CONTENTS

INCIDENCE OF GESTATIONAL DIABETES MELLITUS IN HIV POSITIVE ANTENATAL WOMEN ON ANTIRETROVIRAL THERAPY

ABSTRACT

OBJECTIVES: This is a prospective analytical study to find the incidence of gestational diabetes in 100 HIV positive antenatal women on anti retroviral therapy and to find the association between the antiretroviral regimen used and the occurrence of Gestational diabetes mellitus (GDM).

METHODS: The DIPSI criteria was used to diagnose a patient with GDM. This is a one step glucose challenge test where the patient is given 75g of oral glucose irrespective of fasting state and a 2 hour glucose value greater than or equal to 140mg/dl is diagnostic of GDM.

RESULT: 100 antenatal patients on antiretroviral therapy were taken in this study.The overall incidence of GDM came to 11% in my study. The maternal risk factors that could have caused GDM were as follows. Out of 54 primigravida only 2 had GDM (i.e.) 3.7%, second gravida were a total of 39 patients of which 5 women (12.8%) had GDM, and 3rd gravid out of 6 patients 2 had GDM (33.3%). We had one 4th gravid and she had GDM (100%).As the number of living children increase, the risk of GDM increases, in primigravida the risk was 4.6% and in mulligravida it was 68.2%. In my study I had 3 patients with history of IUD /still birth of which 2 women had GDM (66.7%)Of 4 patients with a history of previous GDM, 3 patients 75% had recurrent GDM. Of 4 patients with BMI >30, 2 patients had GDM (50%)

17 Patients had 1st degree relative with diabetes of which 6 patients (35.3%) had GDM. A history of big baby (Bwt >4kg) is a proven risk factor for GDM. In my study, 3 patients had history of previous baby birth weight >4kg of which 2 patients had GDM in this pregnancy. The risk is 66.7% . The 100 patients in my study, fall into 3 different antiretroviral regimens.

Tenofovir, Lamivudine, Lopinavir – 1 patient ,Tenofovir, Lamivudine ,Efavirenz - Had majority patients, 81 patients of which 9 had GDM (11.1%) Zidovidine, lamivudine, Nevrapine 18 patients of which 1 patient (5.6%) had GDM.There was no significant association between GDM (P value 0.782)and the regimens used in my study.96 patients had live birth of which 7 patients (7.3%risk) had GDM..2 patients had IUD of which 1 patient (50% risk) had GDM and 2 patients had still birth of which both the patient (100%) had GDM.The mean age of patients with GDM is 29.10 yrs (S.D. $\pm$ 3.3)and the mean BMI is 27.85 (SD $\pm$ 3.633)The mean weight gain in patients with GDM is 9.8kg and the mean CD4 count for patients with GDM is 699.40.The univarite analysis shows statistical significance between GDM and parity, previous history of GDM, previous birth weight >4 kg, BMI >30, previous IUD / Still births and a 1st degree relative with GDM.Multivariate analysis (logistic regression) was used and it was found that previous IUD/still birth (OR=89.299), present pregnancy weight gain (OR=3.588) and 1st degree relative with diabetes (OR=18.298) were significant associated with variables in predicting the occurrence of GDM.

CONCLUSION

There is no significant increase in the overall incidence of GDM in HIV patients. Statistically, there is no significant association between the antiretroviral drugs used in my study and the GDM incidence ($p>0.05$).By logistic regression, my study has proven that a history of 1st degree relative with diabetes, previous IUD/still birth and weight gain in this pregnancy are significant variables contributing to GDM in the 11 patients in my study.

Keywords: HIV, Gestational diabetes mellitus , anti retroviral therapy, protease inhibitors, newer regimen.

INTRODUCTION

Transmission of HIV during antenatal period from mother to baby is the key mode in which children acquire HIV. Annually about 14,000 new HIV infections occur in India among children. About 10,000 deaths from HIV infection occur among children in India. United Nations General Assembly adopted a policy towards elimination of pediatric HIV by 2015.India has adopted the same policy. Anti retroviral treatment is the way to this achieve this goal.

Earlier Nevirapine and protease based inhibitors had been used .

The PI-based regimen can reduce the risk of drug resistance and side effects from Nevirapine. The PI-based regimens have been highly successful in controlling HIV viral load and can reduce vertical viral transmission but their benefits are compromised by numerous undesirable side effects.

These include tissue insulin resistance and overt hyperlipidemia, which may be aggravated by the normal physiologic changes of carbohydrate and lipid metabolism during pregnancy. Impaired fetal growth also has been concerned because higher incidence of low birth weight was reported.

Based on the new NACO guidelines december 2013

- Pregnant women newly diagnosed with HIV are started on Tenofovir, Lamivudine, Efavirenz irrespective of CD4 count or clinical stage.
- If a patient is already on a particular ART regimen the same is continued.
- If a patient is already exposed to NNRTI (Nevirapine),the risk of resistance to efavirenz based therapy is high. So in such patients protease inhibitor based regimen is started – Tenofovir, Lamivudine, Ritonavir / Lopinavir.

Aim of the study

AIM OF THE STUDY

To study the incidence of Gestational diabetes mellitus in antenatal mothers diagnosed with HIV and who are on Anti retroviral therapy.

To study the association between Anti Retroviral regimens and occurrence of Gestational Diabetes Mellitus

Materials and Methods

MATERIALS AND METHODS:

STUDY DESIGN

PROSPECTIVE ANALYTICAL STUDY

SETTING:

INSTITUTE OF OBSTETRICS AND GYNECOLOGY

EGMORE, CHENNAI-8.

SAMPLE :

100 HIV positive pregnant women on Anti retroviral therapy for a period from september 2014 to august 2015

MATERIALS AND METHODS:

100 pregnant women infected with HIV and on Antiretroviral therapy for prevention of vertical transmission of HIV at Institute of Obstetrics and Gynaecology, Egmore from September 2014 to August 2015.

The women who had pregestational diabetes or received corticosteroids during pregnancy were excluded from the study. One hundred cases met the criteria. They were closely monitored during pregnancy. The information recorded including HIV history, obstetric data, GDM risk factors (previous GDM, BMI ≥ 30 kg/m2, 1st degree relative with DM, history of stillbirth , previous birth weight > 4,000 gm, body mass index (BMI), total weight gain

and adverse drug effect from prior to current regimens. In addition to routine prenatal blood test, fasting blood sugar, CD4 count, viral load was done.

Screening for GDM with the DIPSI criteria had been done on all HIV-positive pregnant women at 16 weeks, 24-28 weeks and 32 weeks. The patients were given 75-g oral glucose irrespective of fasting state and a cut off of $\geq$ 140 mg/dL was diagnostic of GDM.

The patients were followed upto 6 weeks after delivery and various details collected.

INCLUSION CRITERIA:

- Patients not on corticosteroids
- Patients not a known case of type 2 DM
- Willing for follow up

EXCLUSION CRITERIA:

- Patients on corticosteroids
- Patients who are Pregestational diabetics
- Not wiiling for follow up

EXPECTED OUTCOME OF THE STUDY:

- Protease inhibitor based antiretroviral therapy is known to cause glucose intolerance in patients
- To come up with incidence of GDM in patients on antiretroviral therapy at IOG and to study their association with GDM.

Review of Literature

REVIEW OF LITERATURE

The emergence and pandemic of acquired immunodeficiency syndrome has posed a great challenge to public health in recent times. After sudden appearance of syphilis in Europe five hundred years ago,Rarely has any disease had such great impact on medicine, science and society and caused so much panic among public and government all over the world as AIDS. The full impact of the disease is not known for many years because of silent spread and evolution of this disease.

The first report of this disease came in 1981 from two cities, Los Angeles and New York .There was a unexplained sudden occurrence in large numbers of two uncommon illness in homosexual young adults and drug addicts, namely Kaposi‘s sarcoma and pneumocyctis carinii pneumonia. These patients had no immunity left in their body and hence became susceptible to many life threatening infections and malignancies by relatively avirulent organisms . The above condition was called as Acquired Immunodeficiency syndrome(AIDS)

In 1985 serological test namely ELISA was discovered for detection of antibodies against HIV . This helped further in an accurate estimation of the extent of the infection. Till then , the infection could be diagnosed only when patients developed the characteristic clinical features such as opportunistic

infections or malignancies. These end stage cases represented only tip of the iceberg. Serological testing of high risk groups, blood donors and others revealed a very large reservoir of HIV in patients and carriers all over the world. The rate of infection has been steadily mounting over the years. The saddest part is that the developing world has to carry the brunt of this disease.

HIV VIRUS

HIV causing AIDS belongs to the subgroup lentivirus of Retroviridiae family

Structure:

HIV is a spherical enveloped virus 90-120mm in size The nucleocapsid is made of

- an outer shell which is icosahedral
- an inner core which is cone shaped . It encloses the ribonucleoproteins.

The genome has two positive sense RNA copies which are single stranded and identical, hence diploid .The reverse transcriptase enzyme which is the characteristic feature of this virus is present along with the viral RNA.

Once the virus infects a host cell the viral RNA is first transcribed by the enzyme into single stranded DNA and it is then transcribed into a double stranded DNA This then integrates into the host cell chromosome to form the provirus which has the capability to stay latent for a long time in the host cell During that period it continuously affects the host cell function In response to

stimulation by viral promoters the pro virus begins viral replication by initiating the synthesis various components including viral RNA During viral replication naked virus buds out of the host cell surface membrane During this process it acquires a lipoprotein envelope, of which lipid is derived from surface membrane of host cell and the glycoprotiens are virus coded The virus coded envelope proteins include surface projecting knob like spikes and transmembrane anchoring pedicles The surface spikes bind to the CD4+ receptors on the susceptible host cell Transmembrane pedicles cause cell fusion.

VIRAL GENES AND ANTIGENS:

The genome of HIV has three structural genes (gag,pol,env) characteristic of all retroviruses . It also has other regulatory and non structural genes which are specific for the virus . The products of the genes both the structural and non structural act as antigens. The sera of infected persons contain antibodies to them. Detection of these antigens and antibodies is useful in the diagnosis and prognosis of HIV infection.

***GENES CODING FOR STRUCTURAL PROTIEN*:**

1. The g*ag* gene codes for viral shell and core . It is present as p53 a precursor protein . This p53 is cleaved into p15, p18 and p24 which make up viral core and shell. The major core antigen p24 can be detected in serum even before antibodies can appear. Later in course of

infection there is decline of p24 antibodies . The re-appearance of p24 antigen in circulation denotes exacerbation of the illness.

2. The *env* gene codes for the synthesis of envelope glycoprotein gp160,which is then cleaved into gp 120 which contributes to the surface spikes and gp 41 that forms a transmembrane anchoring protein The glycoprotein gp 120 is the major envelope antigen. Antibodies to gp 120 antigen are seen in circulation till the end stage of the disaese.

3. The *po*l gene codes for the polymerase reverse transcriptase It also codes for other enzymes like endonuclease and protease. It is present as precursor protein which is then divided into proteins p31,p51 and p66.

NON STRUCTURAL PROTEINS:

- *Tat* (trans activating gene) enhancing expression of all viral genes.
- *Nef* (negative factor gene) down regulating viral replication.
- *Rev* (regulator of virus gene) enhancing expression of structural proteins.
- *Vif (* viral infectivity factor gene)influencing infectivity viral particles.
- *Vpu (*is present in HIV1) and *vpx* (present in HIV2) enhances maturation and release of the progeny viruses from the cells
- *Vpr* stimulating the promoter region of the virus

- *LTR (* LONG TERMINAL REPEAT) containing sequences giving promoter enhancer and integration signals.

HIV 1 strains have been classified into atleast 10 subtypes . These subtypes are grouped under A to J and form Group M(major) these cause majority of HIV1 infections all over the world. Subtype A is most common worldwide. Subtype B is most common in America and Europe . The most common subtypes in Africa are A,C and D while in Asia most common subtypes are E ,C and B. Subtype E is prevalent in Thailand. In India and China subtype C is the most common.

PATHOGENESIS:

HIV virus causes infection by entering through blood or tissues of a person it then comes in contact with a susceptible host cell which is mainly the CD4 lymphocyte .

CD4 Lymphocyte is the recptor for the virus and hence the virus infects any cell that bears CD 4 antigen on its surface

Envelope glycoprotein gp120 causes Specific binding of the virus to the CD4 receptor of the host cell . However cell fusion is necessary for infection to take place. This is by gp41 transmembrane protein.Co receptor molecules, CXCR4 for T cell tropic virus and CCR5 for macrophage tropic virus are also necessary for cell fusion and virus entry

After viral fusion with the host cell the HIV genome is uncoated and internalized into the cell The reverse transcriptase enzyme transcribes viral RNA into double stranded DNA. This ds DNA with the help of the enzyme integrase is integrated into the genome of the infected host cell , thus resulting in latent infection in the meanwhile, there is lytic infection from time to time which releases the progeny virions that infect other cells. In an affected individual HIV can be detected from lymphocytes , breastmilk , blood, cervical secretions ,tears, saliva, semen urine and cell free plasma

The main pathogenesis in HIV infection is the virus destroying the CD4 lymphocytes The T4 cells decrease and T4:T8 cell ratio is reversed. Viral

infection can suppress the function of infected cells without causing structural damage. Infected T4 cells do not produce normal amount of gamma interferon, IL-2 and other lymphokines. This markedly decreases the cell mediated immunity.

Though cellular mediated immune response is largely affected humoral mechanism also seems to be influencd to an extent. Helper T cell activity is needed for optimal B cell function, especially in responding to thymus dependent antigen. Hence patients having AIDS are not able to respond to new antigens.

An important feature of AIDS is polyclonal B cell activation resulting in hypergammaglobulinemia . All classes of immunoglobulins are involved but levels of IgG and IgA are raised. In infants and children additionally IgM levels are also elevated. The hypergammaglobulinemia is more of a hindrance than a help because they are mostly useless immunolglobulins to irrelevant antigens and autoantibodies. This may also be responsible for Type 3 hypersensitivity allergic reactions due to immune complexes.

Monocyte - macrophage function is also affected mainly due to decreased secretion of activating factors by the T lymphocytes resulting in decreased chemotaxis ,antigen presentation and intracellular killing by monocytes macrophages . The activity of natural killer cells and cytotoxic T lymphocytes are also affected. The principal immunological abnormalities seen in HIV are:

Features that characterize AIDS are:

- Lymphopenia
- Selective T cell deficiency- reduction in number of CD4 cells ,inversion of T4:T8 ratio
- Decreased delayed hypersensitivity
- Hypergammaglobulinemia - especially IgG and IgA and IgM in children.
- Polyclonal activation of B cells and increased spontaneous secretion of Ig

Other consistently observed features:

- Decreased in vitro lymphocyte proliferative response to mitogens and antigens.
- Decreased cytotoxic response by T cells and NK cells
- Decreased antibody response to new antigens
- Altered monocyte macrophage function
- Elevated levels of immune complexes in serum.

HIV IN PREGNANCY

INCIDENCE:

According to WHO 35.3 million people were living with HIV in 2012 which is an increase from the previous years as more people are receiving antiretroviral therapy There were 2.3 million new HIV infections globally which is a 33% decline from 2001 In USA the number of new cases of HIV has decreased significantly. Advancement and availability of treatment has decreased the rate of mother to child transmission of the disease, has given control over the progression of the disease and the development of opportunistic infections and full blown AIDS. In contrast in the third world the number of deaths and vertical transmission has increased. The advances in therapy have no effect in the poorer countries due to lack of accessibility of these drugs. Worldwide 25-30% of HIV infected patients are women of which 90% of them are in the age group of 20-49 years.

MATERNAL INFECTION:

Maternal HIV infection is acquired mainly by sexual contact or by transfusion. The exact incidence of HIV in pregnancy is unknown. But the fact remains that the incidence is on the rise in developing and developed countries. In most Asian countries the infection rate is less than 0.5% . Studies have demonstrated that pregnancy does not affect the progression or the survival of HIV infected women. Whereas there are debates regarding the effect of HIV

infection on pregnancy outcome. The main association of HIV are preterm birth and fetal growth restriction. However there can be multiple confounding factors like alcohol use, drug abuse ,advanced maternal disease and malnutrition.

IMPLICATION FOR FETAL INFECTION:

Almost 15-25% of babies born to HIV positive mothers show presence of the disease by 1 year of age. The virus is secreted in breast milk and hence breast feeding is contraindicated in HIV. In non breast feeding mothers 60-70% of transmission occurs during delivery while the rest occurs antepartum.

The factors which lead to fetal infection can be classified into maternal and fetal factors.

Maternal factors include severity of disease assessed by CD4+ count or by measuring viral RNA copies. The presence of maternal antibodies against certain epitopes or against the principal neutralizing domain of the envelope protein gp120 is predictive of the absence of infection in the newborn. The number of RNA copies correlates with the risk of vertical transmission. In infected women if the viral load is less than 1000 copies /ml risk of transmission is 0-10%, 17% with viral load of 1000-10,000 copies,33% if load more than 10,000 copies.

The guidelines to start anti retroviral therapy in pregnant women is CD4 count <400/mm^3 or a viral load of >1000 copies/ml by PCR assay. This viral

load is the threshold recommended by ACOG for the performance of cesarean delivery. A CD4 count <200/mm^3 is an indication for prophylactic treatment for opportunistic infections.

With respect to obstetrical factors, the frequency of vertical transmission increases with the duration of ruptured membranes and cesarean delivery has a protective effect. The frequency of vertical transmission decreases if the mother is on HAART (Highly Active Anti Retroviral Therapy) lowers the risk of vertical transmission to the baby irrespective of the maternal viral load, 1% in cases of <1000 RNA copies/ml,6% with levels 1000-10,000 RNA copies/ml and 13% if RNA copies >10,000 copies/ml.

Most of the infants born to HIV positive mothers exhibit no signs of infection. A few of them may have features of HIV embryopathy , characterized by growth retardation, craniofacial abnormalities and microcephaly. Most of the infants born to HIV positive mothers are seropositive when born due to passive transfer of maternal antibodies. But these antibodies gradually decline and disappear by 6 months of age.

United Nations General Assembly adopted a resolution to work towards elimination of pediatric HIV by 2015.Government of India is committed to this goal

MANAGEMENT:

The most important issues in the management of HIV is the detection. CDC recommends screening for HIV for antenatal mothers in their first visit. Thereafter their management involves a multidisciplinary approach involving social workers, obstetrician , paediatrician,nutrtionalists and many other health care providers. If an HIV infected mother decides to continue her pregnancy she needs to have regular CD4 counts and ultrasound to monitor the growth of the fetus.

DRUGS USED ANTIRETROVIRAL THERAPY:

NUCLEOSIDE AND NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS:

- **Zidovudine, Lamivudine, Stavudine, , Abacavir,** Emtricitabine**,** Didanoside **Tenofovir (NtRTI).**

NON NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS:

- **Efavirenz ,Nevirapine**

INTEGRASE INHIBITOR*:*

- Raltegravir

FUSION INHIBITOR:

- Enfuviritide

PROTEASE INHIBITOR:

- **Ritonavir, Lopinavir, Atazanavir**, Nelfinavir, Saquinavir, Indinavir, Amrepinavir, Fosamprenavir , Tipranavir , Darunavir

ENTRY INHIBITORS(CCR5/CXCR4 antagonists)

Maroviroc.

*The drugs which are highlighted are available in the NACO ART programme.

NRTI:

Zidovudine (AZT, ZDV)

- Effective against HIV-1 & 2
- Available as tablet and syrup
- Reduces the rate of vertical transmission
- Adult Dose: 300mg twice daily
- Available as Fixed Dose Combination in the National ART programme
- Preferred over Tenofovir in first line ART in HIV patients having Haemoglobin >9G%

Stavudine(D4t)

- Effective against HIV-1 & 2
- High oral bioavailability
- Available as tablet (for adults and children)
- Adult Dose: 30mg twice daily
- Stavudine has been phased out of first line ART regimens in children and adults

- Stavudine administration is reserved for the alternate / second line regimens [in the inevitable situations with the approval of State AIDS Clinical Expert Panel (SACEP)]

Lamivudine (3TC)

- Effective against HIV-1 & 2 and HBV
- Excellent drug, well tolerated and least toxic
- Synergistic action with Zidovudine & Stavudine
- Low genetic barrier for resistance
- Lamivudine resistant mutants reduce viral fitness
- Adult Dose: 150mg twice daily
- Available as Fixed Dose Combination in the National ART programme

TOXICITIES OF NRTIs

DRUGS	ZIDOVUDINE	STAVUDINE	LAMIVUDINE
SHORT TERM	Headache ,nausea vomiting, malaise diarrhea, bone marrow suppression, anemia(macrocytic)		Skin rash (very rash)
MEDIUM TERM	bone marrow suppression, anemia, hyperpigmentation, lactic acidosis	lactic acidosis, peripheral neuritis, pancreatitis	
LONG TERM		Lipodystrophy, dyslipedemia	

ABACAVIR(ABC):

- Abacavir is available along with Lamivudine (3TC) in formulations of 60/30 mg and 300/150 mg
- Can be taken with meal
- Common side-effects are nausea vomiting Malaise Headache & Diarrhoea
- No dose adjustment in renal failure
    - but the combined formulations (with 3TC) are NOT to be used in patients with creatinine clearance less than 50 ml/min.
- Major complication: Hypersensitivity reaction
- Abacavir hypersensitivity is linked to HLA-B 5701 gene
- <5% of adults and children
- Usually during first 6 weeks of therapy, but may occur at any time!
- Rash, fever, fatigue, diarrhoea, vomiting, abdominal pain, arthralgia, respiratory symptoms, increased liver enzymes, lymphadenopathy, mucus membrane ulcerations
- Potentially fatal
- STOP Abacavir and NEVER restart

NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITOR(NtRTI)

TENOFOVIR:

- Mechanism and site of action similar as NRTIs (Already in mono phosphate form, need only diphosphorylation whereas other NsRTIs need triple phosphorylation)
- Potent drug against HIV-1 & 2 and HBV
- Usually well tolerated; Flatulence may bother some
- Nephrotoxicity: low incidence; Fanconi syndrome (hypophosphataemia, hyperuricemia, proteinuria, normoglycaemic glycosuria) and rarely Acute Renal Failure
- Can reduce bone mineral density
- Adult dose: 300 mg tablet once daily

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIS)

- Non-competitively block Reverse Transcriptase at the active site at a distinct point from NRTIs
- Active against HIV-1 replication cycles as NRTIs
- Not active against HIV-2 replication cycles
- Inducers of the hepatic cytochrome P450 enzyme system (CYP3A4 and others) – leading to many drug interactions

- Primarily excreted via hepatic route
- NNRTIs in Programme: Nevirapine and Efavirenz

NEVIRAPINE:

- Active against HIV-1; Not active against HIV-2
- Excellent oral bioavailability, not food dependent
- Nevirapine is a substrate and potent inducer of the hepatic cytochrome P450 enzyme system (CYP3A4 & others) leading to many drug interactions
- Single dose 200mg is effective in prevention of HIV transmission from mother to newborn and is being administered at the time of labour
- Preferred NNRTI in First line ART (except when patient is on Rifampicin containing ATT for co-infected TB)

EFAVIRENZ

- Active against HIV-1; Not active against HIV-2
- Oral bioavailability increased with fat meal
- Adult dose 600mg at bed time
- Metabolised by Cytochrome P450 enzyme system; however, Rifampicin reduces bioavailability of Efavirenz only by 20%

- Preferred during treatment for TB (with Rifampicin); Adult dose of Efavirenz remains the same-600mg
- Avoid in children:
    - <3 years of age
    - When Body Wt <10 kg
- CNS toxicity: Vivid dreams, nightmare, dizziness, headache, , depression, insomnia, exacerbation of psychiatric disorders, psychosis, suicidal ideation hallucination, impaired concentration and attention span
- CNS effects (at least some) are observed during first few doses of Efavirenz in >50% of patients
    - Typically starts after 1st and / or 2nd dose of Efavirenz
    - Usually subsides by 2 to 6 weeks
- Risk factors:
    - Genetic predisposition
    - Use of concomitant drugs with CNS effects
    - Efavirenz is to be taken in empty stomach before night dinner or 2-3 hours after dinner before going to bed to reduce drug concentration and CNS effects
    - Pre-existing psychiatric illness

NNRTI ADVERSE EFFECTS

DRUG	ADVERSE EFFECTS
ALL NNRTIs	Skin rash, hepatitis, CNS manifestations
NEVIRAPINE	Hepatitis,skin rash,steven jhonson syndrome,
EFAVIRENZ	Confusion, abnormal thinking, agitation, anxiety. Fetal malformation during first four weeks of gestation, Gynecomastia in a small proportion of patients.

PROTEASE INHIBITORS:

- Protease Inhibitors prevent splitting of large viral precursor proteins into functional core proteins
- Produce immature, defective, noninfectious viral particles
- Extensively metabolised by cytochrome P450 enzyme system (CYP3A4 and others)
- Atazanavir + Ritonavir or Lopinavir + Ritonavir (Boosted PI is being used for Alternate first line ART and Second line ART in India

RITONAVIR BOOSTED PROTEASE INHIBITOr:

- The primary role of Ritonavir in boosted protease inhibitor regimen is to enhance the pharmacokinetics of the second PI
- It is achieved by inhibiting of CYP3A4. The resultant increase in Cmax, Cmin and AUC of the second Protease inhibitor (Atazanavir or Lopinavir) enhance its the therapeutic bioavailability
- Ritonavir boosted PI (e.g. Atazanavir/ritonavir and Lopinavir/ritonavir) regimens have shown high levels of viral load suppression among both antiretroviral naïve and prior PI-treated patients
- Raises the genetic barrier for development of PI resistance
- Reduces pill burden

PROTEASE INHIBITORS SIDE EFFECTS:

Side effects	Management
Dyslipidemia (hypertriglyceridemia, hypercholesterolemia) & Lipodystrophy	Diet, walking, statins, Fenofibrate, etc.
Rise of transaminase (10-12%)	Screen for HbsAg & anti-HCV & monitor LFTs regularly
Hyperglycemia	Diet control, OHA, Insulin
Increased bleeding episodes in Haemophiliacs	Frequent Factor VIII transfusion
Osteoporosis, avascular necrosis	Switching to non-PI based ARV, Calcium supplementation

Atazanavir (ATV):

- Activity against HIV-1; variable activity against HIV-2
- Administration with food enhances bioavailability
- Atazanavir is largely metabolised in the liver by cytochrome P450 (CYP) 3A and inhibits CYP3A and UGT1A1
- Atazanavir boosted with Ritonavir
- Dose Atazanavir (300mg) + ritonavir (100mg) OD
- Renal failure Standard dose can be used except in patients on haemo-dialysis who should get only boosted atazanavir

PI-class specific side-effects:

- Hyperglycemia, fat maldistribution, hyperlipidemia (especially with Ritonavir boosting)
- Increased bleeding episodes in haemophiliacs
- Unique side-effects of Atazanavir include
- Indirect Hyperbilirubinaemia (producing yellow discolouration of sclera)
- Skin rash
- Nephrolithiasis (rare)
- Hepatic failure having Child-Pugh Score 7-9, dose is 300mgs once daily; avoid with score >9
- If Indinavir and Atazanavir are taken together can cause Indirect hyperbilirubinemia, . Hence, Indinavir should not be co administered concomitantly
- Atazanavir is a Category B drug in Pregnancy (FDA)
- Atazanavir is not recommended for use in patients less than 6 years of age

LOPINAVIR (LPV)

- Activity against HIV-1 and against HIV-2
- Lopinavir is extensively metabolised in the liver by cytochrome P450 (CYP) 3A and inhibits CYP3A and UGT1A1
- Lopinavir is boosted by co-administered Ritonavir
- Dose 400 mg of LPV/100mg of RTV twice daily in adults and as per weight bands in children
- Oral LPV/r syrup formulation is available for administration in children; should be given with food
- A high-fat meal increases absorption of this drug, especially of the liquid preparation

Operational Guidelines For Lifelong ART For All Pregnant Women Living With HIV To Prevent Mother To Child Transmission Of HIV In India.

December 2013 NACO GUIDELINES:

The anti retroviral therapy helps the mother by improving her own health and also helps in PPTCT programme by reducing the viral load in mother and loading the newborn with the virus. Providing Nevirapine syrup to newborn upto 6 weeks after birth helps in prohylaxis to the newborn: If a woman is newly diagnosed as HIV positive she is started immediately on ART. If she is already on a particular regimen of ART the same is continued throughout pregnancy.

RECOMMENDATIONS FOR HIV POSITIVE PREGNANT WOMEN

Pregnant women newly detected to be HIV positive during routine antenatal check up should be initiated on Anti Retroviral Therapy regardless of clinical stage or CD4 count.

TDF tenofovir (300mg) + 3TC lamivudine (300mg) + EFV efavirenz (600mg)

Obtain sample for CD4 count before initiating or soon after starting ART The initiation of ART should not be delayed for want of CD4 test results.

ART regimen for pregnant women having prior exposure to NNRTI for PPTCT

Because of the risk of resistance (archived resistance) to NNRTI drugs in this population, Efavirenz in the TDF+3TC+EFV regimen may not be effective. Thus, these women will require a protease inhibitor-based ART regimen **TDF(tenofovir)+ 3TC(lamivudine) + LPV(lopinavir)**

As per PPTCT guidelines, all positive pregnant women exposed to NVP in past should be initiated on LPV (lopinavir)/ritonavir instead of EFV.

The indications for Cotrimoxazole initiation in pregnant women follow that for other adults. Cotrimoxazole prophylaxis prevents Opportunistic Infections (OIs) such as Pneumocystis jiroveci pneumonia (PCP), toxoplasmosis, diarrhoea as well as bacterial infections.

Cotrimoxazole should be given if CD4 count <250 cells/mm^3. It should be continued through pregnancy, delivery and breast-feeding as per national guidelines. It should be ensured that the pregnant women takes her folate supplements regularly.

INTERVENTIONS DURING LABOUR AND DELIVERY:

- Minimise vaginal examinations
- Avoid prolonged labour by using oxytocin to shorten labour
- Avoid premature rupture of membranes

  Use partogram to monitor labour

  Do not use suction unless absolutely necessary
- Avoid unnecessary trauma during delivery
  - Use non-invasive foetal monitoring
  - Avoid invasive procedures
  - Avoid routine episiotomy
- Try to avoid the use of forceps or vacuum
  - Avoid Uterine manipulation- external cephalic version (ECV)

Caesarean section performed prior to the onset of labour and rupture of the membrane minimises HIV transmission.

The risk of elective Caesarean for reducing mother to child transmission should be assessed carefully in the context of factors such as, risk of post-operative complications and Cost

In India normal vaginal delivery is recommended unless the woman has obstetric indications for a C-section.

Use of ART can reduce risk of mother to child transmission is better and with less risk than a C-section.

For infants:

- Observe for signs and symptoms of HIV infection
- All HIV exposed infants should receive cotrimoxazole at 4-6 weeks of age
- Follow standard immunisation schedule
- Routine well baby visits
- Early Infant Diagnosis: DNA PCR test
- 18-month visit for HIV antibody testing

Feeding practices:

- Feeding options must be explained to all the mothers and they must be allowed to select their choice
- Exclusive Replacement feeding (ERF) if Affordable, Feasible, Acceptable, Sustainable & Safe

Breastfeeding: NACO Recommendations: –

HIV positive:

For these infants, exclusive breast feeding is to be done till 6 months. Breast feeding can be continued up to 12 months.

HIV negative:

Exclusive breast feeding is to be done till 6 months and start complimentary feeding at 6 months of age. Breastfeeding should continue up till 12 months only. Stopping of breast feeding should be done gradually over 1 month according to the comfort of the mother and child. Educate parents that HIV testing needs to be done again after cessation of breastfeeding according to the EID protocols.

PROPHYLAXIS FOR HIV EXPOSED INFANTS:

BIRTH WEIGHT	DOSE	DURATION
<2KG	2MG/KG ONCE A DAY	6 WEEKS
2-2.5KG	10MG PER DAY	6WEEKS
>2.5KG	15 MG PER DAY	6WEEKS

1) Gestational Diabetes mellitus in a cohort of HIV-1 infected pregnant women

MI Gonzalez Tome and associates, HIV medicine Vol.9, Issue-10, Pages 868-874, Nov.2008.

This is a prospective analytical study conducted in 12 spanish hospitals in urban areas of Madrid and Barcelona from may 2000 to December 2003. The cohort had 669 HIV positive pregnant women. The aim was to find the prevalence of gestational diabetes mellitus (GDM) and associated risk factors in these patients.

None of the mothers had were on pentamidine corticosteroids or other drugs (except ARV) which affects glucose metabolism. Women with pregetational diabetes were excluded from the study. A variety of information was gathered including clinical events in pregnancy, obstetric and demographic details, insulin use, ART history and HIV history

Additional screening for Hep B, Hep C, rubella, CMV & genital infections was done. Screening for GDM using O'Sullivan test at 24-26 hours and confirmation with oral glusose challenge test was done.

Results

The median age was 30.7 years (range 16-44) At third trimester median viral load was 1.910g (range 1.7-5.4) . and CD4 count was 545 cells/µl (range 139-1690 cells)

74% of patients were on HAART of which 41% were on protease inhibitor.

An above average prevalence of 7% for GDM was found 95% confidence internal (CI) 5.2-9.5 Risk factors associated with GDM in univariate analysis include protease inhibitor exposure hepatitis C co-infection older age stavudine However Protease inhibitor(AOR 2.4, 95%) CI (1-5.3) and older age (adjusted to odds ratio (AOR) 1.09, 95% CI (1-1.1) were proven as independent risk factors in multivariate analysis for GDM development.

2) Effect of antiretroviral agents on carbohydrate metabolism in HIV-1 infected pregnant women.

Patricia E1 Beitune and associates.

Diabetes / Metabolism Research and Reviews. Vol 22, Issue 1, Pages 59-63, January / February 2006.

A prospective analytical study was conducted on 57 pregnant women to find the effect of antiretroviral drugs (ARV) on the carbohydrate metabolism in pregnancy.

The women were divided into 3 groups ZDV group 20 HIV-1 infected women taking zidovudine TT group 25 patients on triple antiretroviral (ZDV + 3TC + NFV) and control group 12 pregnant women.

Fasting plasma glucose and OGTT were performed on these patients.

Results

The median values of the area under the curve (AUC) of glycemic values over a period of 120 min between the 33rd and 38th week was 136.50mg/dL for the TT group(p0.049) 134.77 mg/dL for ZDV group 116.85 mg/dL for control group There was an increase in AUC along pregnancy for all three groups regardless of the treatment used although this increase was significant only in the TT group (p-0.001) The antiretroviral agents had no deleterious effects on low birth weight prematurity on Apgar scores or intrauterine growth restriction.

Conclusion

There was an association noted between the use of protease inhibitors and the development of glucose intolerance in pregnancy The antiretroviral drugs had no deleterious effect on perinatal prognosis.

3) The AMRO study Pregnancy outcomes in HIV 1 infected women under effective HAART and a policy of vaginal delivery

K. Boer, D Patel and associates BJOG, Vol 114, Issue 2, Pg 148-155, Feb 2007.

A cohort of 143 HIV positive pregnant women including matched case control study in a 2:1 ratio of controls to case (n=98) was conducted at Academic Medical Centre in Amsterdam and Erasmus Medical Centre in Rotterdam from December 1997 to July 2003 All HIV infected women on HAART and delivery after 15 weeks were included in the study.

Patient characteristics like ethinicity, age, mother's testing, type of HAART, time of inhibition, maternal viral loads, CD4+ count were collected.

Result

MTCT was 0% [95% CI (0.2%)]. 78% of HIV-1 positive women had commenced and 62% delivered vaginal delivery Preterm delivery rates were 18% (95% CI 11-27) in women infected with HIV-1 and 9% (95% CI 5-13) in controls (p=0.03) The calculated number of caesarean sections needed to prevent single MTCT was 131 or more HAART used at <13 weeks of gestation was associated with a 44% preterm delivery rate compared with 21% when

HAART was started at or after 13 weeks and 14% in controls incidence of pre-eclampsia and Very low birth weight were not different between HIV1 and controls.

4) Improved Obstetric outcomes and few maternal toxicities associated with antiretroviral therapy, including highly active antiretroviral therapy during pregnancy.

Juomala, RuthE, Watts D Heather and associates Journal of AIDS, 1 April 2005, Vol.38, Issue 4, P 449-473

It was a multicentric, prospective, cohort study of 2543 HIV positive pregnant women and their infants that began enrollment in 1989 all singleton pregnancies that ended between January 1990 and Feb 2002 were included . Delivery >20 weeks of gestation were included.

Prospective data collected consisted of patient, interviews, standardized laboratory data assessment, medical records abstraction, CD4 count and HIV viral load were measured.

Information regarding time of initiation of ART at time of enrollment collected.

The ART regimen used was also noted for each case.

Outcome Definitions

Maternal complications included gestational diabetes (diagnosed based on 3 hr GTT) anemia (Hct <28 or Hb <9.3) thrombocytopenia (Platelet count <100000) gastrointestinal toxicities (Pancreatitis, cholecystitis / cholelithiasis, esophagitis, gastritis, hyperemesis, hepatitis or abnormal liver function tests in absence of chronic hepatitis) neurological toxicities (seizures, subarachnoid hemorrhages, subdural hematoma, cerebral atrophy and motor symotoms, renal toxicities, dermatological toxicities lactic acidosis and death obstetric complications included hypertensive complications (BP>140/90, albuminuria, HELLP) preterm labour, PPROM, preterm delivery, low birth weight, stillbirth.

Statistical Methods

Distribution and means of maternal characteristics according to timing and type of ART were compared using X^2 analysis. ART variables and non ART co-variables related to the outcomes were determined through univariate analysis using countingency table analyses for categoric exposure variables , student t test for continuous variables Logistic regression using a stepwise elimination procedure was performed to identify independent predictors of each specified outcome

Odds ratio and 95% CI were obtained from X^2 analysis and final logistic regression model

Results

Late use of ART was associated with GDM OR=3.5 95% CI 1.2-10.1 ART use was associated with anemia OR=1.6 95% CI : 1.1-2.4 There was an increase in preterm delivery <37 weeks in 10 women with late use of ART not containing zidovidine OR=7.9 95% CI 1.4-44.6 There was a decrease in adverse pregnancy outcome as follows.

Late use ART containing zidovidine associated with decreased stillbirth OR=0.06 95% CI 0.02 – 0.18 and preterm delivery at <37 weeks OR=0.5 95% CI 0.3-0.8

ART containing nucleoside reverse transcriptase inhibitors but not ZDV during early and late pregnancy was associated with decreased risk for Preterm delivery at <32 weeks (OR=0.3, 95% CI=0.2-0.7).

Benefits of ART continue of overweight observed risk.

5) Effect of protease inhibitor therapy on glucose intolerance in pregnancy

Jang, Jennifer & associated, Obstetrics and Gynaecology May 2006, Vol 107, Issue 5.

The objective of this study was to find if protease inhibitor use was associated with increased glucose intolerance in HIV positive pregnant women

Method :

The study included 171 HIV positive pregnant women from January 1, 1998 to January 8 2004 who had 1 hour and 3 hour glucose test values

available History of drug regimens used at the time of glucose testing was noted. HIV infected women were then matched 1:3 to HIV non infected pregnant women by race, age and 1 year of delivery.

Results:

171 HIV women has glucose test available. 12% had an abnormal 1hr glucose value 3% had abnormal 3 hour glucose. This was similar to HIV non infected women 45% of HIV infected cohort was on protease inhibitor at the time of glucose testing. Protease inhibitor exposure has no effect on glucose test and HIV infection also had no effect on glucose test results.

6) Pregnancy complications in HIV positive women – 11 year data from Frankfurt HIV cohort

Reitter, Stucker AU, LindeR and associates; HIV med 2014 oct.

The aim of this study was to analyse the pregnancy complications in HIV positive women and changes in the rates of such complications over 11 years in Frankfurt A cohort of 330 HIV positive women between January 1 2002 to 31 December 2012 were included in this study The incidence of pregnancy related complications such as preeclampsia mode of delivery,, preterm delivery, gestational diabetes and obstetric history were analysed. Maternal and neonatal mortality and morbidity as well as HIV mother to child transmission were evaluated.

Results:

In this study 5 women 1.5% developed preeclampsia Gestational diabetes was diagnosed in 38 women 11.4% In 16 women 4.8% preterm rupture of membranes (PROM) occurred 46 women were admitted with preterm labour Preterm delivery rate was 36.5% . 26.9% of deliveries (n=90) were between 34 weeks and 36+6 weeks The percentage of women with undetectable HIV viral load had increased significantly $p<0.001$ from 26.1% to 75% leading to obstetric changes including an increase in rate of vaginal deliveries ($p<0.001$) from no vaginal births to 50% The preterm delivery rate decreased significantly ($p<0.501$) from 79.2% to 8.3% There was no significant changes in PROM, preeclampsia,GDM or preterm labour.

7) Gestational Diabetes Mellitus and Dyslipidemia in HIV infected pregnant women receiving protease inhibitors based HAART.

Nahawut Wetchitticharеon, Suvanna A Savapiriyanont. Thai journal of Obstetrics and Gynaecology, January 2013, Vol 21, PP 10-15.

The objective of the study was to find the incidence altered lipid metabolism gestational diabetes mellitus (GDM) and birth weight in HIV infected pregnant women receiving protease inhibitor based HAART.

This is a cross sectional descriptive study involving 109 HIV infected pregnant women on Protease inhibitor based (Lopinavir / Ritonavir) HAART to prevent mother to child transmission at Rajanithi Hospital the study was conducted from October 2010 to July 2012 A 100g glucose tolerance test was

performed in women with abnormal OGCT values during 2nd and 3rd trimester and lipid profile was measured after the 4th week of treatment.

The women who had pre-gestational diabetes for those on corticosteroids were excluded from the study.

Birth weight, apgar scores and route of delivery were recorded. All statistical analysis were performed using SPSS 16.0 software.

Results :

The patients mean age was 28.9 years, most (79.8% were have for HAART before pregnancy. The incidence of GDM was 7.3%. There was an increase in post treatment level of total cholesterol (TC) and triglyceride at 18.9 mg/dL (95% CI (9.5-28.4) and 97.2 mg/dL (95% CI 70.9 – 123.3) respectively. The incidence of low birth weight was 17.4%.

Conclusion:

Use of protease inhibitors based HAART in pregnant women was associated with increased GDM and altered lipid metabolism.

8) Gestational Diabetes Mellitus in HIV infected and uninfected pregnant women in Cameroon.

Jenifer Goa, Marcia Wong and associated Diabtes care 2013 september 36(9) e141-e142. Published online 2013 August.

A prospective analytical study of 316 pregnant women aged 15-50 years at a large semiurban clinic in Cameroon was conducted. A 75g OGTT was performed at 24-28 weeks or at first prenatal visit for those who came after 28 weeks Data on height, blood pressure, socio demographic obstetric history, pre pregnancy weight, HIV status, anti-retroviral therapy and pregnancy, outcomes collected Exact logistic regression models were used to identify and study the variables predicting GDM.

Of 316 participants 3 had overt diabetes and 20 (6.3%) had GDM. Women with GDM presented for OGTT later than those without GDM (p=0.04). After adjustments for family history of diabetes gestational age at the time of OGTT pre pregnancy BMI ,age only age >30 years, remained a significant predictor of GDM Among HIV infected women 6.6% (11 of 166) exhibited GDM In this subgroup median age 30.5 vs 28 yrs systolic 118 vs 105 mmHg and diastolic 76 vs 64mmHg blood pressure and rates of Combined ART use during pregnancy 90.9 vs 54.2% differed significantly between those with vs without GDM (P=0.04 0.02 0.02 respectively)

Overall rate of GDM (6.3%) is comparable with those is developed settings These are very much dependent on method and criteria used. The use

of combined ART particularly protease inhibitors is associated with GDM in pregnancy and non pregnant women The low rates of Combined ART (33 of 166) and protease inhibitor (1 of 166) use in HIV infected group explains why an association between HIV and GDM was not found in this study.

Among HIV infected group GDM was associated with high blood pressure. Almost all (91%) of the HIV infected women with GDM were on Combined ART.

Nonetheless, the significant association between Combined ART and GDM in univariate analysis is consisted with reports in developed countries.

Observation & Results

STATISTICS

TABLE 1: PARITY AND GDM

			GDM		
			NO	**YES**	**Total**
Gravid	1	Count	52	2	54
		% within gravid	96.3%	3.7%	100.0%
		% within gdm	57.8%	20.0%	54.0%
		% of Total	52.0%	2.0%	54.0%
	2	Count	34	5	39
		% within gravid	87.2%	12.8%	100.0%
		% within gdm	37.8%	50.0%	39.0%
		% of Total	34.0%	5.0%	39.0%
	3	Count	4	2	6
		% within gravid	66.7%	33.3%	100.0%
		% within gdm	4.4%	20.0%	6.0%
		% of Total	4.0%	2.0%	6.0%
	4	Count	0	1	1
		% within gravid	.0%	100.0%	100.0%
		% within gdm	.0%	10.0%	1.0%
		% of Total	.0%	1.0%	1.0%
	Total	Count	90	10	100
		% within gravid	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	15.353[a]	3	.002
Likelihood Ratio	10.399	3	.015
Linear-by-Linear Association	11.185	1	.001
N of Valid Cases	100		
a. 4 cells (50.0%) have expected count less than 5. The minimum expected count is .10.			

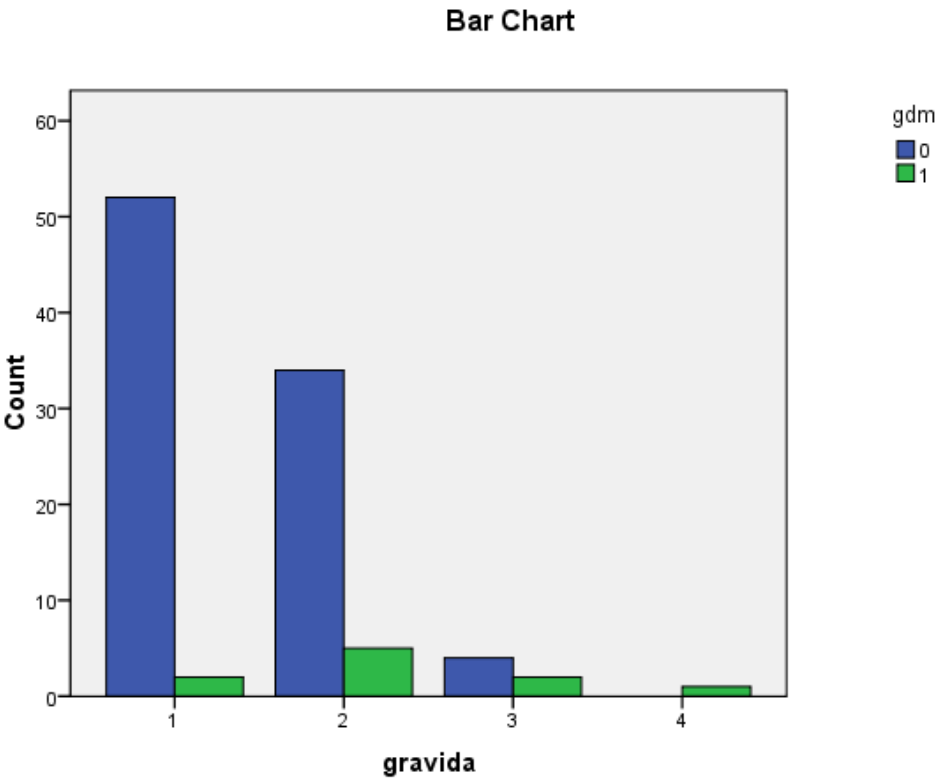


Table1 shows that as the parity increases there is a steady increase in the risk for GDM, primigravida has a risk of 3.7%,second gravida 12.8%, third gravida 33.3%, fourth gravid is almost 100%. The P value is <0.05(0.015) satistically significant

TABLE 2: LIVE BIRTH

			GDM		
			0	**1**	**Total**
live birth	0	Count	62	3	65
		% within live birth	95.4%	4.6%	100.0%
		% within gdm	68.9%	30.0%	65.0%
		% of Total	62.0%	3.0%	65.0%
	1	Count	27	6	33
		% within live birth	81.8%	18.2%	100.0%
		% within gdm	30.0%	60.0%	33.0%
		% of Total	27.0%	6.0%	33.0%
	2	Count	1	1	2
		% within live birth	50.0%	50.0%	100.0%
		% within gdm	1.1%	10.0%	2.0%
		% of Total	1.0%	1.0%	2.0%
	Total	Count	90	10	100
		% within live birth	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.104[a]	2	.017
Likelihood Ratio	6.637	2	.036
Linear-by-Linear Association	7.447	1	.006
N of Valid Cases	100		

a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is .20.

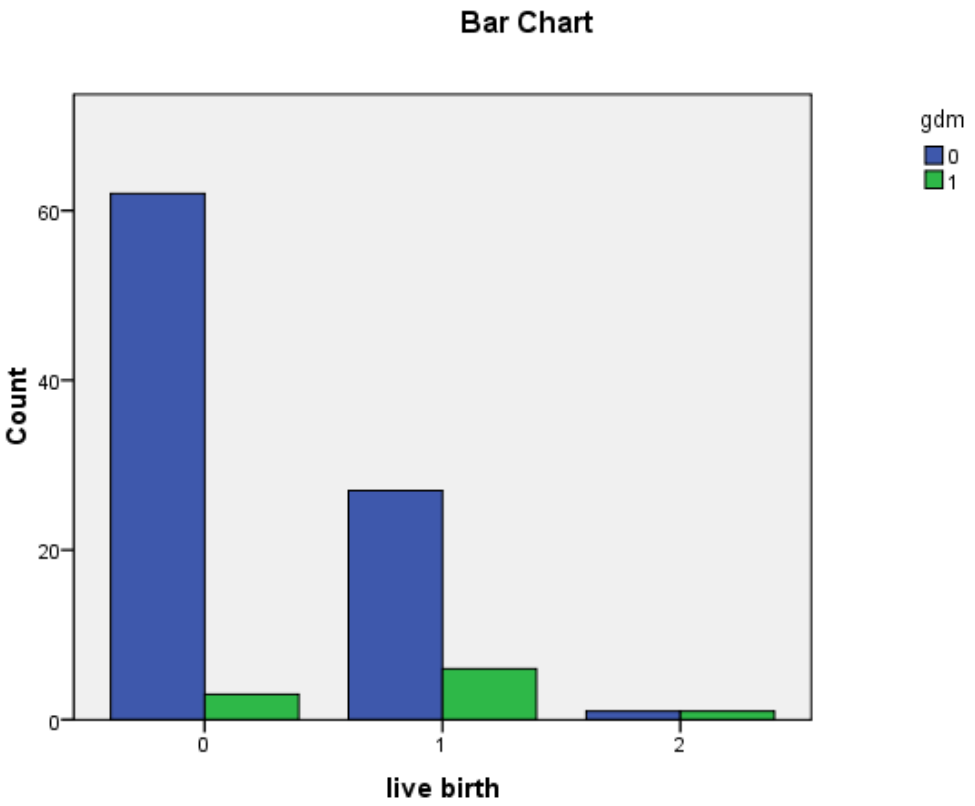


Table 2 shows that as the number of living children increases the risk for GDM also increases. It is 4.6% in primigravida and 50% in multigravida. P value is 0.036 (<0.05) statistically significant.

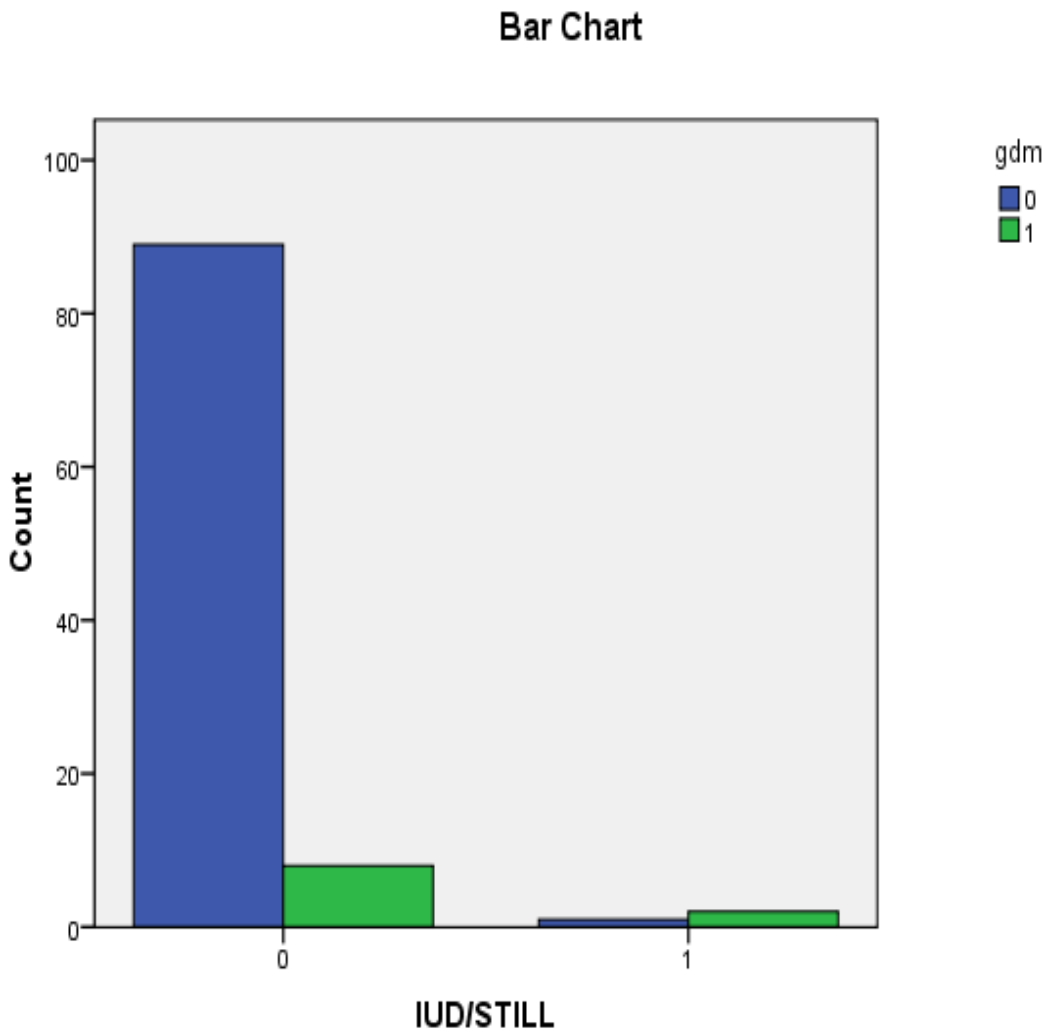
TABLE 3 : PREVIOUS IUD/STILL BIRTH

			GDM		Total
			NO	YES	
IUD/STILL	NO	Count	89	8	97
		% within IUD/STILL	91.8%	8.2%	100.0%
		% within gdm	98.9%	80.0%	97.0%
		% of Total	89.0%	8.0%	97.0%
	YES	Count	1	2	3
		% within IUD/STILL	33.3%	66.7%	100.0%
		% within gdm	1.1%	20.0%	3.0%
		% of Total	1.0%	2.0%	3.0%
	Total	Count	90	10	100
		% within IUD/STILL	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	11.035[a]	1	.001		
Continuity Correction[b]	5.498	1	.019		
Likelihood Ratio	5.952	1	.015		
Fisher's Exact Test				.026	.026
Linear-by-Linear Association	10.924	1	.001		
N of Valid Cases	100				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .30.

b. Computed only for a 2x2 table



This table shows that the risk of GDM with previous IUD or still birth is increased to 66.7%. The P value is <0.05%(0.015) which is statistically significant.

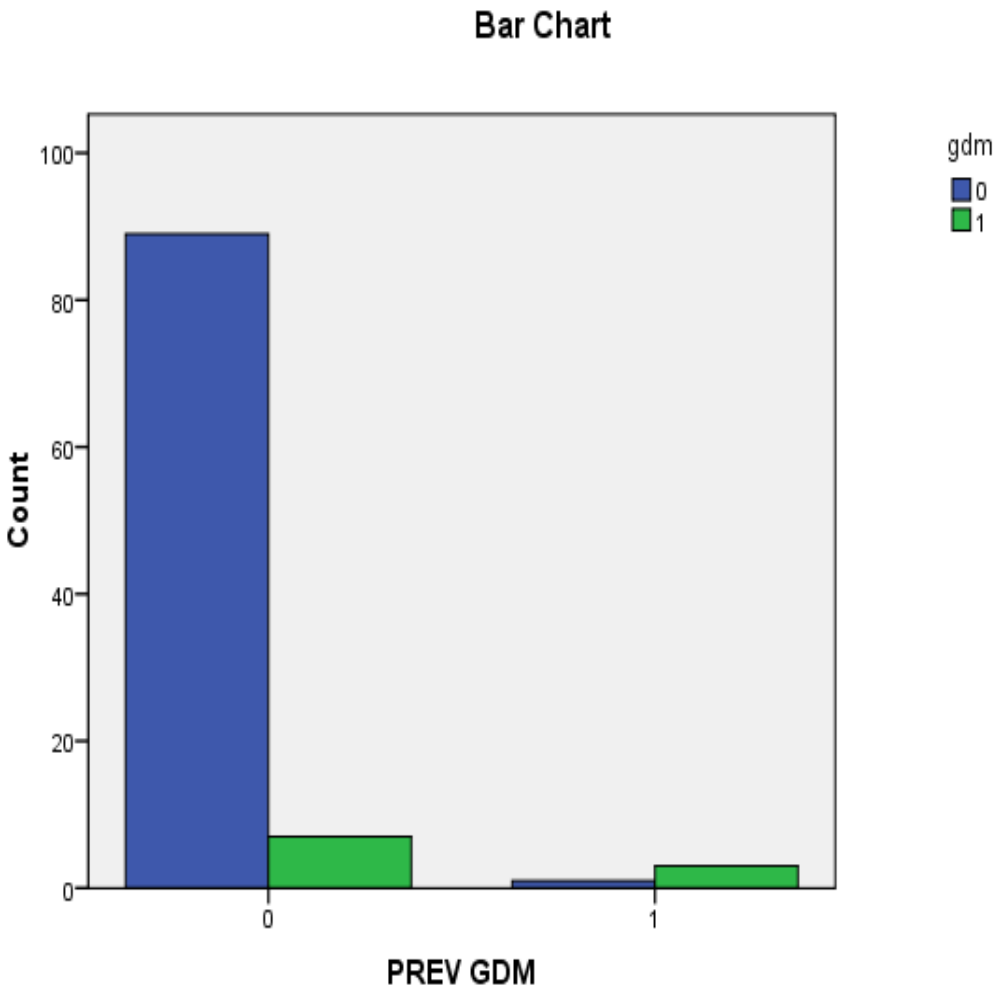
TABLE 4 : PREV GDM

			GDM		
			NO	**YES**	**Total**
PREV GDM	No	Count	89	7	96
		% within PREV GDM	92.7%	7.3%	100.0%
		% within gdm	98.9%	70.0%	96.0%
		% of Total	89.0%	7.0%	96.0%
	Yes	Count	1	3	4
		% within PREV GDM	25.0%	75.0%	100.0%
		% within gdm	1.1%	30.0%	4.0%
		% of Total	1.0%	3.0%	4.0%
	Total	Count	90	10	100
		% within PREV GDM	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	19.560[a]	1	.000		
Continuity Correction[b]	12.760	1	.000		
Likelihood Ratio	10.383	1	.001		
Fisher's Exact Test				.003	.003
Linear-by-Linear Association	19.365	1	.000		
N of Valid Cases	100				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .40.

b. Computed only for a 2x2 table



This table shows that the risk of GDM increases by 75% if there is a previous history of GDM.The P value is 0.001(<0.05) statistically significant.

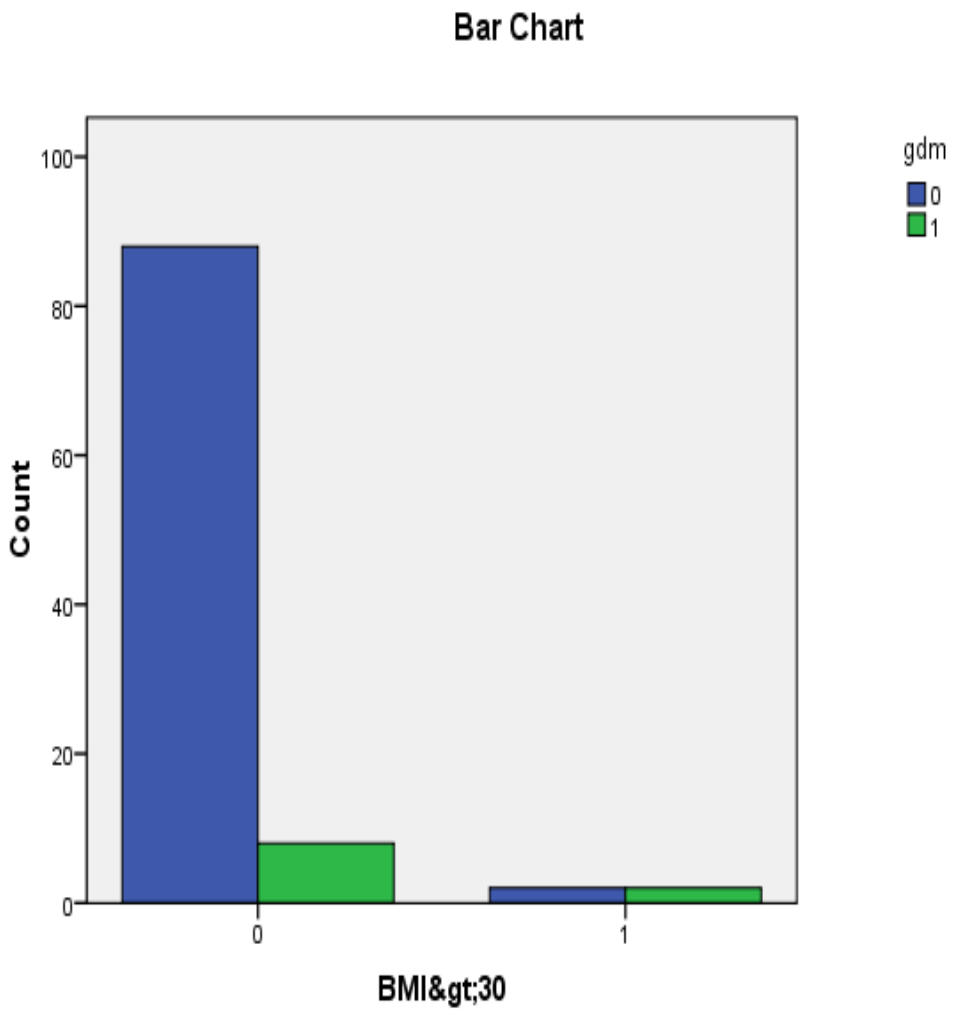
TABLE 5 : BMI>30 * GDM

			GDM		Total
			0	**1**	
BMI>30	0	Count	88	8	96
		% within BMI>30	91.7%	8.3%	100.0%
		% within gdm	97.8%	80.0%	96.0%
		% of Total	88.0%	8.0%	96.0%
	1	Count	2	2	4
		% within BMI>30	50.0%	50.0%	100.0%
		% within gdm	2.2%	20.0%	4.0%
		% of Total	2.0%	2.0%	4.0%
	Total	Count	90	10	100
		% within BMI>30	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	7.407[a]	1	.006		
Continuity Correction[b]	3.501	1	.061		
Likelihood Ratio	4.399	1	.036		
Fisher's Exact Test				.049	.049
Linear-by-Linear Association	7.333	1	.007		
N of Valid Cases	100				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .40.

b. Computed only for a 2x2 table



This table shows that the risk of GDM increases by 50% if BMI is greater than 30. P value is 0.036 (<0.05) which is statistically significant.

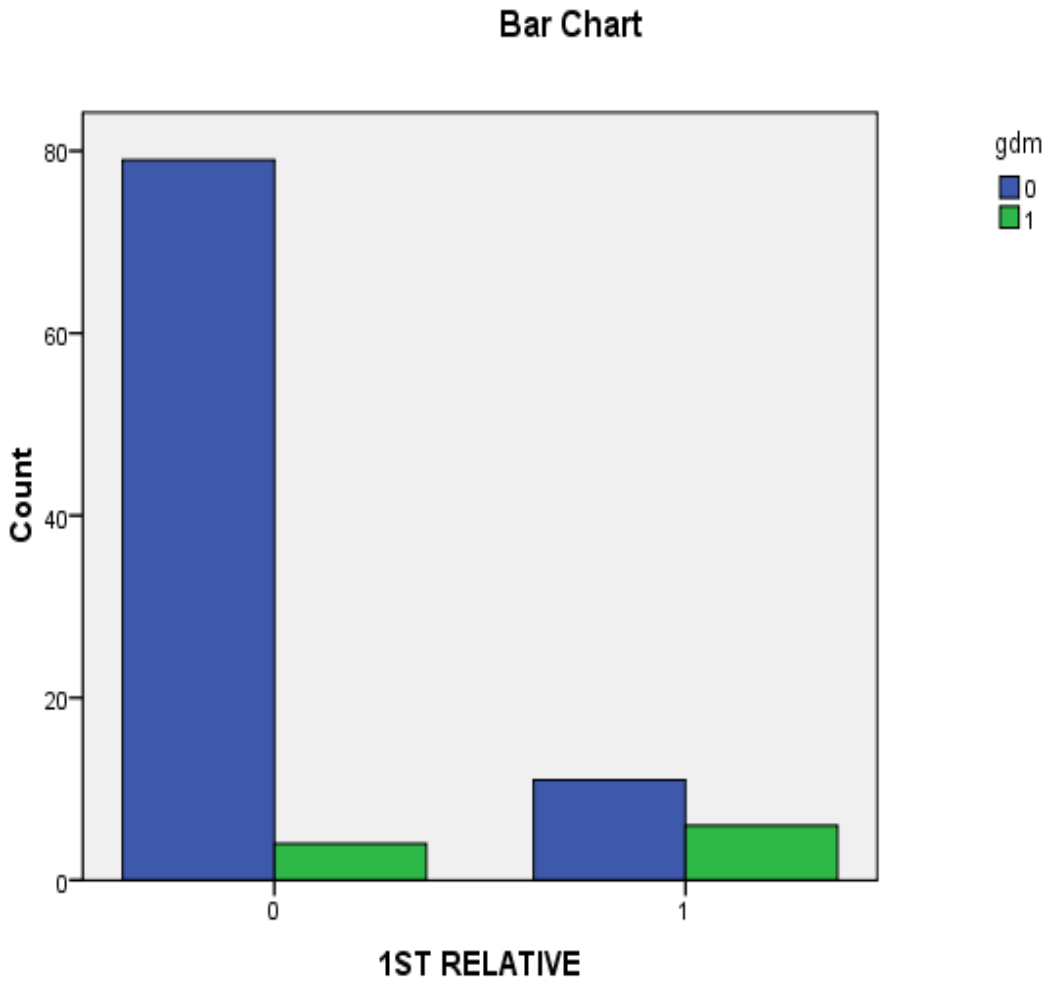
Table 6:1ST RELATIVE * gdm

			GDM		
			0	**1**	**Total**
1ST RELATIVE	0	Count	79	4	83
		% within 1ST RELATIVE	95.2%	4.8%	100.0%
		% within gdm	87.8%	40.0%	83.0%
		% of Total	79.0%	4.0%	83.0%
	1	Count	11	6	17
		% within 1ST RELATIVE	64.7%	35.3%	100.0%
		% within gdm	12.2%	60.0%	17.0%
		% of Total	11.0%	6.0%	17.0%
	Total	Count	90	10	100
		% within 1ST RELATIVE	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests					
	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	14.560[a]	1	.000		
Continuity Correction[b]	11.371	1	.001		
Likelihood Ratio	10.878	1	.001		
Fisher's Exact Test				.001	.001
Linear-by-Linear Association	14.415	1	.000		
N of Valid Cases	100				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 1.70.

b. Computed only for a 2x2 table



Presence of a first degree relative with diabetes increases the risk of GDM by 35.3%

P value is <0.05(0.001) which is statistically significant.

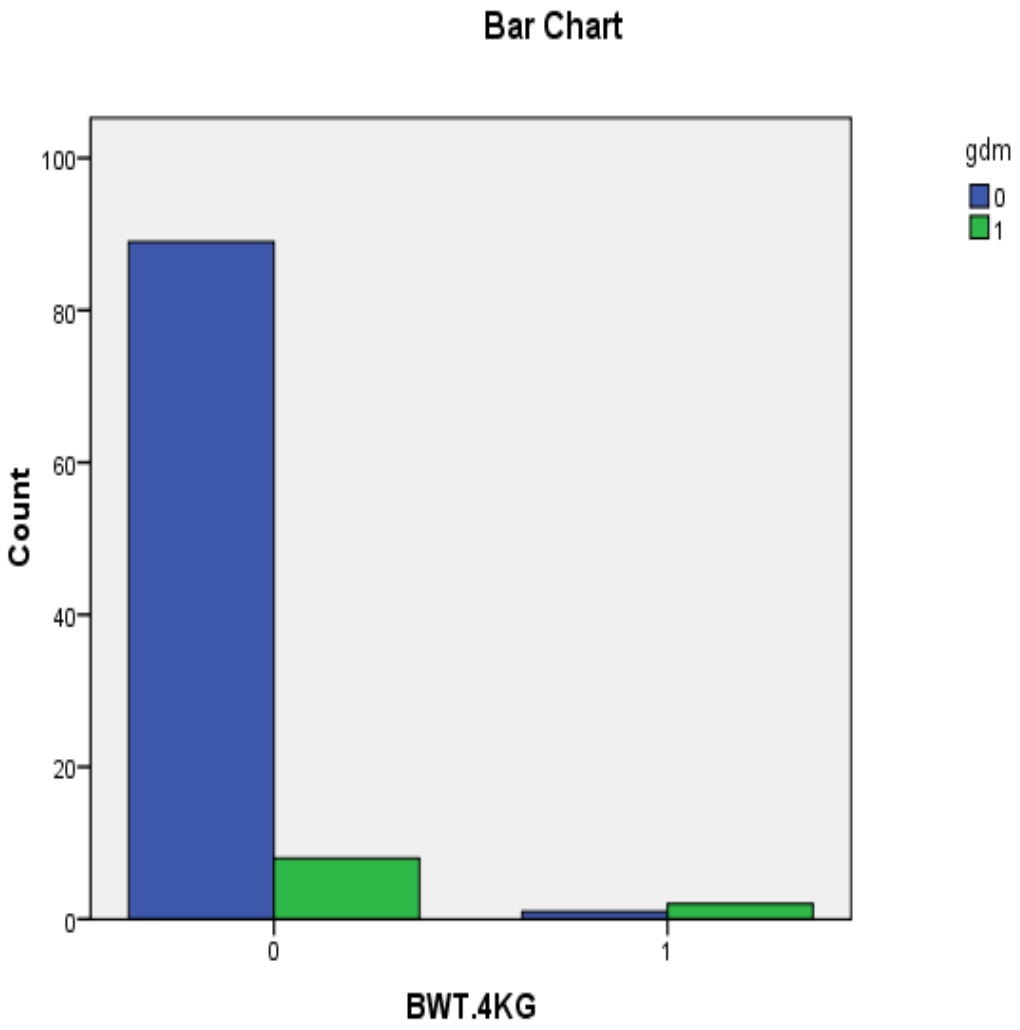
TABLE 7 : BWT.4KG * GDM

			GDM		TOTAL
			0	**1**	
BWT.4KG	0	Count	89	8	97
		% within BWT.4KG	91.8%	8.2%	100.0%
		% within gdm	98.9%	80.0%	97.0%
		% of Total	89.0%	8.0%	97.0%
	1	Count	1	2	3
		% within BWT.4KG	33.3%	66.7%	100.0%
		% within gdm	1.1%	20.0%	3.0%
		% of Total	1.0%	2.0%	3.0%
	Total	Count	90	10	100
		% within BWT.4KG	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests					
	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	11.035[a]	1	.001		
Continuity Correction[b]	5.498	1	.019		
Likelihood Ratio	5.952	1	.015		
Fisher's Exact Test				.026	.026
Linear-by-Linear Association	10.924	1	.001		
N of Valid Cases	100				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .30.

b. Computed only for a 2x2 table

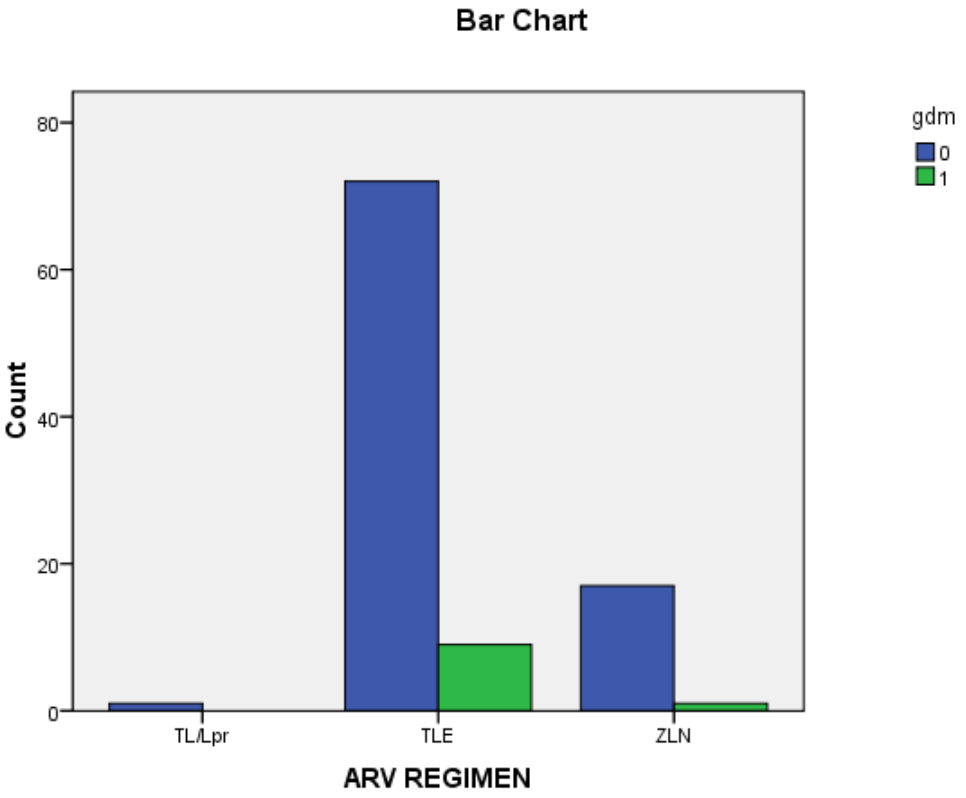


A previous baby with birth weight >4 kg increases the risk of GDM by 66.7% . P value is 0.015(<0.05) which is statistically significant.

TABLE8 : ARV REGIMEN * GDM

			GDM		Total
			0	1	
ARV REGIMEN	TL/Lpr	Count	1	0	1
		% within ARV REGIMEN	100.0%	.0%	100.0%
		% within gdm	1.1%	.0%	1.0%
		% of Total	1.0%	.0%	1.0%
	TLE	Count	72	9	81
		% within ARV REGIMEN	88.9%	11.1%	100.0%
		% within gdm	80.0%	90.0%	81.0%
		% of Total	72.0%	9.0%	81.0%
	ZLN	Count	17	1	18
		% within ARV REGIMEN	94.4%	5.6%	100.0%
		% within gdm	18.9%	10.0%	18.0%
		% of Total	17.0%	1.0%	18.0%
	Total	Count	90	10	100
		% within ARV REGIMEN	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.617[a]	2	.734
Likelihood Ratio	.782	2	.676
N of Valid Cases	100		
a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is .10.			

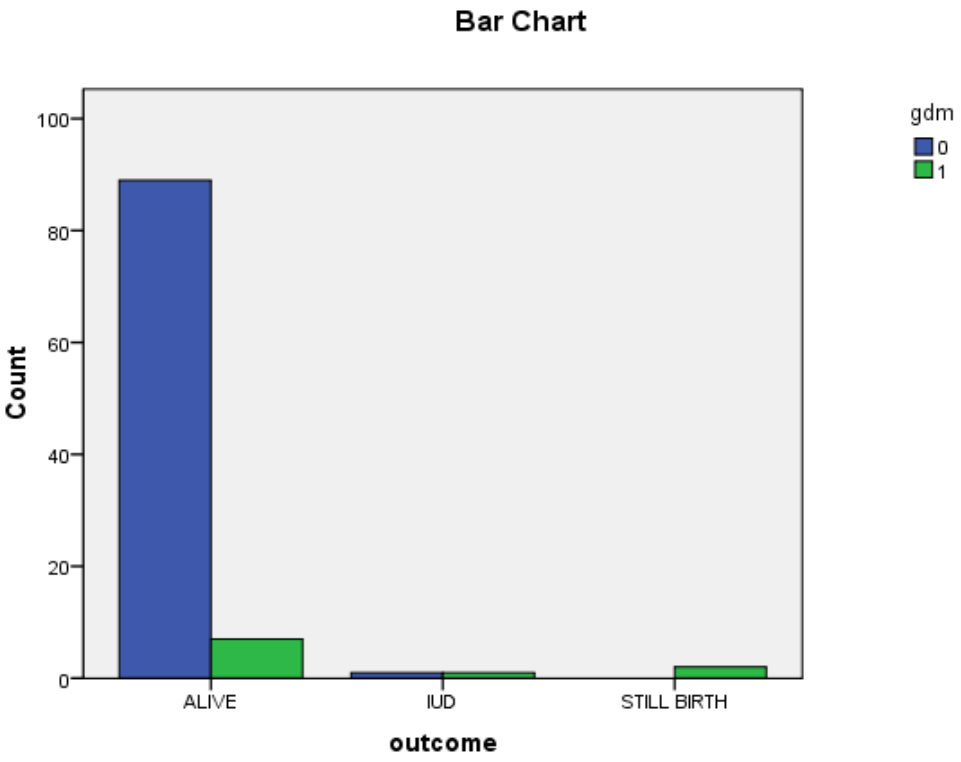


11.1% of patients on TLE developed GDM and 5.6% of patients on ZLN had GDM. Occurence of GDM had no statistical significance [pvalue 0.782(>0.05)] with the occurrence of GDM in these patients.

Table09:Outcome of this pregnancy:

			GDM		Total
			0	1	
Outcome	ALIVE	Count	89	7	96
		% within outcome	92.7%	7.3%	100.0%
		% within gdm	98.9%	70.0%	96.0%
		% of Total	89.0%	7.0%	96.0%
	IUD	Count	1	1	2
		% within outcome	50.0%	50.0%	100.0%
		% within gdm	1.1%	10.0%	2.0%
		% of Total	1.0%	1.0%	2.0%
	STILL BIRTH	Count	0	2	2
		% within outcome	.0%	100.0%	100.0%
		% within gdm	.0%	20.0%	2.0%
		% of Total	.0%	2.0%	2.0%
	Total	Count	90	10	100
		% within outcome	90.0%	10.0%	100.0%
		% within gdm	100.0%	100.0%	100.0%
		% of Total	90.0%	10.0%	100.0%

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	22.338[a]	2	.000
Likelihood Ratio	12.109	2	.002
N of Valid Cases	100		
a. 4 cells (66.7%) have expected count less than 5. The minimum expected count is .20.			



The oucome of this pregnancy patients who had live births the risk of GDM was found to be 7.3%, With IUD risk was 50% and with still birth it was 100%

Group Statistics						
	gdm	N	Mean	Std. Deviation	Std. Error Mean	P
AGE	1	10	29.10	3.315	1.048	
	0	90	25.37	2.996	.316	
BMI	1	10	27.850000	3.6338685	1.1491301	
	0	90	23.603333	2.5117007	.2647565	
CD4 COUNT	1	10	699.40	234.479	74.149	
	0	90	628.11	191.601	20.197	
WEIGHT GAIN	1	10	9.800000	1.3165612	.4163332	
	0	90	8.633333	1.4581040	.1536977	

Independent Samples Test					
		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
AGE	Equal variances assumed	.024	.877	3.700	98
	Equal variances not assumed			3.410	10.699
BMI	Equal variances assumed	3.457	.066	4.835	98
	Equal variances not assumed			3.601	9.978
CD4 COUNT	Equal variances assumed	.129	.720	1.092	98
	Equal variances not assumed			.928	10.379
WEIGHT GAIN	Equal variances assumed	.799	.374	2.421	98
	Equal variances not assumed			2.629	11.599

LOGISTIC REGRESSION:

Model if Term Removed[a]					
Variable		Model Log Likelihood	Change in -2 Log Likelihood	df	Sig. of the Change
Step 1	WEIGHTGAIN	-19.372	9.703	1	.002
	gravida	-14.769	.497	1	.481
	IUDSTILL	-16.536	4.032	1	.045
	outcome	-19.190	9.340	2	.009
	PREVGDM	-14.719	.397	1	.529
	@1STRELATIVE	-20.646	12.251	1	.000
Step 2	WEIGHTGAIN	-20.446	11.468	1	.001
	gravida	-15.295	1.168	1	.280
	IUDSTILL	-17.080	4.738	1	.030
	outcome	-19.904	10.385	2	.006
	@1STRELATIVE	-20.824	12.225	1	.000
Step 3	WEIGHTGAIN	-21.744	12.944	1	.000
	IUD/STILL BIRTH	-19.378	8.213	1	.004
	outcome	-21.485	12.427	2	.002
	@1STRELATIVE	-20.645	10.746	1	.001
a. Based on conditional parameter estimates					

Variables in the Equation							
		B	S.E.	Wald	df	Sig.	Exp(B)
Step 3[a]	WEIGHTGAIN	1.278	.539	5.622	1	.018	3.588
	IUDSTILL	4.492	1.843	5.941	1	.015	89.299
	outcome			.368	2	.832	
	outcome(1)	-25.048	26043.464	.000	1	.999	.000
	outcome(2)	-24.053	26043.465	.000	1	.999	.000
	@1STRELATIVE	2.907	1.087	7.155	1	.007	18.298
	Constant	8.866	26043.465	.000	1	1.000	7085.182

a. Variable(s) entered on step 1: WEIGHTGAIN, gravida, IUDSTILL, outcome, PREVGDM, @1STRELATIVE.

We have done the multivariate binary logistic regression analysis and found that previous IUD/STILL birth, Weightgain in the present pregnancy and Ist degree relative were significant associated risk variables in predicting the outcome with their Odds ratio as follows:

1. Weight gain - odds ratio 3.588
2. IUD still - odds ratio 89.299
3. 1st relative - odds ratio 18.298

Discussion

DISCUSSION

100 antenatal patients on antiretroviral therapy were taken in this study.

The overall incidence of GDM came to 11% in my study. *Seshiah et al* [17] conducted a study for prevalence of GDM in Chennai ,results were as follows ;17.8% in urban,13.8% semiurban,9.9% rural.

The maternal risk factors that could have been the cause for GDM were analysed.

- PARITY: Out of 54 primigravida only 2 had GDM (i.e.) 3.7%, second gravida were a total of 39 patients of which 5 women (12.8%) had GDM, and 3rd gravida out of 6 patients 2 had GDM (33.3%). We had one 4th gravid and she had GDM (100%). Chi square test showed a p-value of 0.015 ($p<0.05$) which was statistically significant ,similar to findings of *seshiah et al* .[17]

- As the number of living children increase, the risk of GDM increases, in primigravida the risk was 4.6% and in mulligravida it was 68.2%. pvalue 0.036 (<0.05) statistical significant.

- PREVIOUS IUD/STILL BIRTH : Is a well known risk factor for GDM. In my study I had 3 patients with history of IUD / still birth of which 2 women had GDM (66.7%) The p-value came to 0.015 (<0.05) statistically significant.*McMahon et al* [39] found previous still birth as a significant risk factor[RR 1.8,95% CI 1.08-3.01]

- PREVIOUS GDM: Of 4 patients with a history of previous GDM, 3 patients 75% had recurrent GDM. The p-value by chi square test cause to 0.001% (<0.05) statistically significant. *Stephanie mac neill et al* 35.6% [95% CI=31.9-39.3%] rate of recurrence *of GDM*[38]

- OBESITY BMI >30 :Of 4 patients with BMI >30, 2 patients had GDM (50%) Chi square tests shows p-value of 0.036 (0.05).*Seshiah et al* [17] prevalence of GDM highest if BMI>= 25Kg/m2, 28.4% in urban,23.8%in semiurban and 16.1% in rural. The prevalence of GDM in his study was 75% more in women with BMI>=25 than in women with BMI 23-24.9

- FAMILY HISTORY: 17 Patients had 1st degree relative with diabetes of which 6 patients (35.3%) had GDM. P-value by chi square tests is 0.001 (p<0.05) which is statistically significant.

Similar to findings of *Seshiah et al*[17]family history of diabetes was a significant risk factor for GDM.

- PREVIOUS BIG BABY: A history of big baby (Bwt >4kg) is a proven risk factor for GDM. In my study, 3 patients had history of previous baby birth weight >4kg of which 2 patients had GDM in this pregnancy. The risk is 66.7% p value is 0.015 (>0.05) which is statistically significant. Similar to findings of *McMahon et al* [39]

- The 100 patients in my study, fall into 3 different antiretroviral regimens.

Tenofovir, Lamivudine, Lopinavir – 1 patient,

Tenofovir, Lamivudine ,Efavirenz - Had majority patients, 81 patients of which 9 had GDM (11.1%)

Zidovidine, lamivudine, Nevrapine 18 patients of which 1 patient (5.6%) had GDM.

Nattawut et al [14] in his study of 109 patients on protease inhibitor based HAART had a an incidence of 7.3% of GDM

As the protease based inhibitors is no longer in use after the introduction of new regimen, newer studies with these drugs are still awaited.

There was no significant association between GDM (P value 0.782)and the regimens used in my study.

The outcome of this pregnancy in the 100 patients under study can be summarised as follows;

- 96 patients had live birth of which 7 patients (7.3%risk) had GDM.
- 2 patients had IUD of which 1 patient (50% risk) had GDM and 2 patients had still birth of which both the patient (100%) had GDM.
- The mean age of patients with GDM is 29.10 yrs (S.D. $\pm$ 3.3)(*Robin vergeese et al* [37]median age 27.62+-3.864) and the mean BMI is 27.85 (SD $\pm$ 3.633)[*Robin vergeese et al* [37]mean BMI 27.89+3.48 Kg/m2]
- The mean weight gain in patients with GDM is 9.8kg (*Robin vergeese et al* [37] in his study found 57.65%(128women) of 222

GDM mothers had weight gain between 10 to 20 kg) and the mean CD4 count for patients with GDM is 699.40(.*Gonzlez et*[1] *al* 545cells/microlitre)

- The univarite analysis shows statistical significance between GDM and parity, previous history of GDM, previous birth weight >4 kg, BMI >30, previous IUD / Still births and a 1st degree relative with GDM.

- Multivariate analysis (logistic regression) was used and it was found that previous IUD/still birth (OR=89.299), present pregnancy weight gain (OR=3.588) and 1st degree relative with diabetes (OR=18.298) were significant associated with variables in predicting the occurrence of GDM.

Conclusion

CONCLUSION

- There is no significant increase in the overall incidence of GDM in HIV patients.
- Statistically, there is no significant association between the antiretroviral drugs used in my study and the GDM incidence ($p>0.05$)
- But the 11% incidence of GDM could be explained due to various other risk factors associated with GDM which include obesity, history of GDM in previous pregnancy, history of IUD/still birth and others mentioned in my study.
- By logistic regression, my study has proven that a history of 1st degree relative with diabetes, previous IUD/still birth and weight gain in this pregnancy are significant variables contributing to GDM in the 11 patients in my study.

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Annexures

PROFORMA

1) NAME

2) AGE

3) IP NO

4) PARITY

5) EDUCATION

6) HEIGHT

7) WEIGHT

8) CD4 COUNT

9) TIME OF INITIATION OF ART

10) OBSTRETIC DATA

11) RISK FACTORS FOR GDM

previous GDM,

BMI ≥ 30 kg/m2,

urine glucose ≥ 1+,

1st degree relative with DM,

history of stillbirth ,

previous birth weight >4kg

others

7) TOTAL WEIGHT GAIN

<12:

>OR=12

8) ARV REGIMENS:

NONE

LAMIVUDINE/ TENOFOVIR/EFAVIRENZ

LOPINAVIR/TENOFOVIR/LAMIVUDINE

ZIDOVUDINE/LAMIVUDINE/NEVIRAPINE

TENOFOVIR/LAMIVUDINE/NEVIRAPINE

9) ADVERSE DRUG EFFECT:

10) OGCT :

16 WEEKS

24-28 WEEKS

32WEEKS

11)GTT

FASTING

1HR

2HR

3Hr

12) TREATMENT:

13)CO MORBID CONDITIONS

14)MODE OF DELIVERY

15)BABY DETAILS:

PRETERM

BIRTH WEIGHT

RDS

OTHERS

14)6 WEEKS POST PARTUM SUGAR VALUES

I/We have been explained about the need for screening for GDM and the need to take antiretroviral treatment in my own vernacular language.

After fully understanding it I/We give full consent for the testing without any undue pressure from anybody. I/We do not hold hospital staff or doctors responsible for any untoward complications.

Patient sign

Relative sign

MASTER CHART

S.NO	IP NO	NAME	AGE	PARITY	BMI	CD4 COUNT	ART INITIATION	OUTCOME	EDD	RISK FOR GDM						WEIGHT GAIN	ARV REGIMEN	OGCT			TREATMENT	DELIVERY	BABY				6 WEEKS OGCT
										PREV GDM	BMI>30	1ST RELATIVE	STILL BIRTH	BWT.4KG				1ST VISIT	24-28	32			PRETERM	BIRTH WT	RDS	OTHERS	
1	15860	sachu	23	primi	19.4	342	16.3.13	ALIVE	2.9.14			YES			1	7	TLE	96	94	102		NVD	YES	1.9			
2	16031	Uma	30	G2P1L1	28	727	12.1.13	ALIVE	09.9.14						0	11	TLE	74	92	96		NVD		2.5			
3	16066	sujatha	22	PRIMI	31	435	7.1.13	ALIVE	13.9.14		yes	YES			1	9	TLE	160			insulin	FTLSCS		3.6			84
4	16179	Roja	25	PRIMI	20.5	643	15.1.13	ALIVE	17.9.14						0	10	ZLN	86	84	105		LSCS		2.95			
5	16318	rekha	22	G2A1	23.3	340	18.1.13	ALIVE	21.9.14						0	10.5	TLE	85	95	92		LSCS		3.1			
6	17048	srilekha	24	G2P1L1	26.4	457	28.2.13	ALIVE	22.9.14						0	11.5	TL/Lpr	84	90	78		LSCS		1.75			
7	17461	manjula	26	G2P1L1	24.4	538	23.3.13	ALIVE	26.9.14						0	11	TLE	70	82	76		NVD		2.760			
8	17980	Devi	27	PRIMI	20.7	670	26.2.13	ALIVE	30.9.14						0	8	TLE	75	74	84		NVD		2.200			
9	18004	rekha	23	PRIMI	24.4	893	22.3.13	ALIVE	30.9.14			YES			1	10	ZLN	86	84	90		NVD		2.5			
10	18093	indhra	25	G2A1	22.8	1017	15.1.13	ALIVE	3.10.14						0	10	TLE	75	74	80		LSCS		3.25			
11	19218	karpagam	25	PRIMI	24.6	644	24.2.13	ALIVE	7.10.14						0	11.4	ZLN	90	88	92		LSCS		3.100			
12	19522	bhavani	32	G3P1L1A1	28.6	828	24.3.13	IUD	8.10.14	YES				YES	1	12.5	TLE	102	153		insulin	ftnvd		4.2			80
13	19711	sajitha	26	PRIMI	19.7	85	22.2.13	ALIVE	10.10.14						0	7.4	TLE	90	85	84		NVD		2.750			
14	19860	vanisri	22	PRIMI	24.3	430	20.4.13	ALIVE	13.10.14			YES			1	10.5	TLE	82	90	85		NVD		2.400			
15	19932	swapna	19	PRIMI	20.4	458	18.3.13	ALIVE	15.10.14						0	9.8	TLE	75	70	76		LSCS		2.950			
16	20017	renuga	29	G2P1L1	23.6	645	25.4.13	ALIVE	20.10.14						0	9	TLE	80	75	70		LSCS		3.150			
17	20081	dhivya	27	G2P1L1	30.4	736	13.4.13	ALIVE	23.10.14		YES				1	10	TLE	75	80	82		LSCS		2.800			
18	20102	mariyammal	28	G2P1L1	29.3	658	6.5.13	ALIVE	26.10.14			YES			1	10	TLE	126	147		INSULIN	LSCS		3.9			85
19	20116	logeshwari	26	PRIMI	22.4	347	10.4.13	ALIVE	29.10.14						0	8.5	TLE	80	84	86		NVD		2.400			
20	20180	rehnaz	33	G3P2L2	27.2	472	23.4.13	ALIVE	30.10.14			YES			1	8.5	TLE	74	90	84		NVD		2.890			
21	21057	malliga	21	primi	22.1	649	20.5.13	ALIVE	3.11.14						0	9.5	ZLN	85	96	104		NVD		3.100			
22	21088	vijaylakshmi	28	G2P1L1	24.2	631	4.5.13	ALIVE	9.11.14						0	7.5	TLE	95	96	94		LSCS		3.50			
23	21134	Sony	32	G2P1L1	22.6	834	22.5.13	ALIVE	12.11.14						0	7	TLE	75	76	80		NVD		2.600			

24	21196	suganthi	26	PRIMI	21.2	731	12.5.13	ALIVE	17.11.14						0	8	TLE	80	74	76		NVD		2.550			
25	21200	Devi	23	PRIMI	25.3	640	5.5.13	ALIVE	18.11.14						0	9.5	TLE	92	90	86		NVD		2.450			
26	21249	sangeetha	28	G2P1L1	22.3	452	25.5.13	ALIVE	22.11.14						0	8	TLE	80	92	94		NVD		3.200			
27	21273	nithya	25	PRIMI	21.8	783	7.3.13	ALIVE	23.11.14						0	7	ZLN	93	94	102		NVD		3.00			
28	21337	aishwarya	27	G2A1	21.4	932	12.5.13	ALIVE	26.11.14						0	9	TLE	78	90	79		NVD		3.100			
29	21381	senthamarai	25	G2P1L1	23.7	614	10.5.13	ALIVE	30.11.14			YES			1	9.5	TLE	66	86	80		NVD		2.900			
30	21440	anitha	27	PRIMI	23.5	792	20.5.13	ALIVE	1.12.14						0	7	TLE	84	78	80		NVD		2.400			
31	21593	umarani	29	G2P1L0	22.6	656	24.5.13	ALIVE	2.12.14			YES	YES		1	8	TLE	154			MEAL	LSCS		3.1			84
32	21609	usha	30	G4P3L2	21.7	734	17.6.13	ALIVE	5.12.14	yes		YES	YES		1	8.5	ZLN	142			MEAL	FTNVD		3.2			70
33	1612	puppy	22	G2P1L0	23.2	722	20.6.13	ALIVE	13.12.14				YES		1	8.5	TLE	90	94	90		NVD	YES	2.220			
34	16206	latha devi	23	G2P1L1	22.8	139	12.6.13	ALIVE	17.12.14						0	7.5	TLE	85	80	86		NVD		2.50			
35	21677	murugammal	21	PRIMI	19.3	741	19.4.13	ALIVE	19.12.14						0	6.5	TLE	84	90	92		LSCS		2.750			
36	21702	darisanadevi	32	PRIMI	22.9	540	2.6.13	ALIVE	23.12.14						0	7.5	ZLN	78	82	87		NVD		2.360			
37	21767	srilekha	20	PRIMI	20.1	649	26.5.13	ALIVE	26.12.14						0	8	TLE	90	94	95		NVD		2.500			
38	21804	ammu	21	PRIMI	20.6	637	20.5.13	ALIVE	27.12.14						0	7	TLE	86	82	78		LSCS		3.100			
39	21860	sathya	27	G2P1L1	24.3	953	23.7.14	ALIVE	3.1.15	YES					1	9.5	TLE	65	72	70		LSCS		3.450			
40	22004	gloriya	21	PRIMI	21.7	600	14.7.14	ALIVE	5.1.15			YES			0	8	ZLN	78	70	65		NVD		3.00			
41	22136	nathiya	27	PRIMI	23.8	742	23.8.14	ALIVE	11.1.15						0	7.5	TLE	70	76	74		NVD		3.200			
42	22362	jansi	22	PRIMI	22.1	683	3.8.14	ALIVE	15.1.15						0	7.5	TLE	86	90	92		NVD		2.450			
43	22474	lakshmi	34	G2P1L1	29.8	722	23.8.14	ALIVE	16.1.15						0	11	TLE	95	155		MEAL	FTNVD		3.12			80
44	22576	punithavathy	26	PRIMI	23.9	651	13.8.14	ALIVE	21.1.15						0	7.5	TLE	72	70	74		NVD		2.910			
45	22601	saranya	27	PRIMI	27.5	346	22.8.14	ALIVE	23.1.15						0	8	TLE	68	74	75		LSCS		2.850			
46	23008	revathy	25	PRIMI	23.2	728	19.8.14	ALIVE	25.1.15						0	8.5	TLE	92	90	84		NVD		3.200			
47	23197	nancy	29	G2P1L1	31	244	15.8.14	ALIVE	25.1.15			YES			1	10	TLE	86	146		INSULIN	LSCS		3.5			82
48	23215	baby	25	PRIMI	23.6	326	6.8.14	ALIVE	27.1.15						0	9	TLE	80	84	86		NVD		2.800			
49	23293	brindha	26	G3A2	24.5	469	27.7.14	ALIVE	30.1.15						0	10	TLE	75	80	84		NVD		2.600			
50	24009	shanthy	29	G2P1L1	30.9	185	20.7.14	ALIVE	31.1.15		yes				1	6	TLE	76	89	108		NVD	YES	1.8			
51	24343	kumari	24	PRIMI	19.1	673	12.8.14	ALIVE	2.2.15						0	6.5	TLE	76	80	76		NVD		2.700			
52	24399	prasannadevi	29	G2P1L1	25.6	842	28.8.14	ALIVE	7.2.15						0	8.5	ZLN	84	83	90		LSCS		3.3			

53	25087	merloando	26	G2A1	23.9	936	6.8.14	ALIVE	9.2.15						0	8	TLE	95	104	110		NVD		3.100			
54	24706	sharmila	24	PRIMI	22.6	737	26.8.14	ALIVE	11.2.15						0	7	TLE	86	95	98		NVD		3.250			
55	26259	sumandevi	29	G2P1L1	23.1	491	15.8.14	ALIVE	11.2.15						0	7.5	TLE	84	90	94		NVD		2.450			
56	26702	gowshiya	21	PRIMI	20.6	781	25.8.14	ALIVE	15.2.15			YES			1	6	TLE	78	86	87		NVD		2.500			
57	26901	sumathy	30	G2P1L1	27.8	603	28.8.14	ALIVE	23.2.15						0	8.5	TLE	92	96	95		NVD		2.600			
58	27352	sumandevi	24	PRIMI	23.5	577	24.8.14	ALIVE	27.2.15						0	8	TLE	75	80	84		NVD		2.400			
59	27471	sharmila	25	PRIMI	27.3	765	20.8.14	ALIVE	1.3.15						0	9.5	ZLN	80	86	90		LSCS		2.950			
60	27783	rathi	27	PRIMI	24.6	733	28.8.14	ALIVE	2.3.15						0	8.5	TLE	66	70	74		LSCS		3.200			
61	28194	kamatchi	32	PRIMI	30.2	780	3.9.14	ALIVE	6.3.15						0	10	TLE	89	85	95		NVD		3.300			
62	28553	devi	22	PRIMI	23.7	317	21.9.14	IUD	10.3.15			YES			1	9	ZLN	70	75	76		NVD		3.250			
63	28903	lakshmi	21	PRIMI	22.5	960	11.9.14	ALIVE	11.3.15						0	9.5	TLE	80	85	75		NVD		2.750			
64	29112	christi	26	G2P1L1	26.2	650	22.9.14	ALIVE	15.3.15						0	11	TLE	75	80	84		LSCS		3.250			
65	30035	aruna	22	PRIMI	20.3	844	27.9.15	ALIVE	16.3.15						0	7.5	TLE	86	128	96		NVD		3.00			
66	30209	berenice	27	PRIMI	32	1032	1.9.14	ALIVE	21.3.15		YES				1	10.5	TLE	155			INSULIN	FTLSCS		3.6			80
67	30411	manjula	28	G2P1L1	25.7	370	14.9.14	ALIVE	24.3.15					yes	1	7	TLE	82	84	84		NVD		2.750			
68	30525	preethi	22	PRIMI	19.6	637	1.9.14	ALIVE	31.3.15						0	6	TLE	98	90	96		NVD		2.850			
69	31196	sandiya	25	G2P1L1	23.8	936	28.9.14	ALIVE	3.4.15						0	7.5	TLE	125	98	115		NVD		3.1			
70	32007	sudandra	24	PRIMI	24.5	778	23.9.14	ALIVE	5.4.15						0	8.5	ZLN	97	102	112		NVD		2.5			
71	32960	banupriya	25	G2 P1L1	23.3	420	21.9.14	ALIVE	6.4.15			YES			1	7.5	TLE	84	96	110		NVD		2.6			
72	33014	sagayam	25	PRIMI	22.5	549	1.10.14	ALIVE	10.4.15						0	7	ZLN	110	115	125		NVD		2.95			
73	33206	thamarai	27	G2 P1L1	28.9	646	13.10.14	ALIVE	17.4.15						0	10	TLE	82				NVD		3.00			
74	24	sangeetha	25	PRIMI	24.2	742	17.10.14	ALIVE	18.4.15						0	9.5	TLE	95	86	97		LSCS		2.5			
75	96	lakshmimurugan	29	G2 P1L1	26.9	679	19.10.14	ALIVE	22.4.15						0	9.5	ZLN	90	95	98		NVD		3.1			
76	102	pushpa bai	22	PRIMI	21.3	704	12.10.14	ALIVE	25.4.15						0	7	TLE	96	127	125		NVD		2.890			
77	157	anjana	27	G2P1L1	23.7	437	2.10.10	ALIVE	29.4.15			YES			1	8.5	TLE	83	80	90		NVD		2.75			
78	190	padmavathy	27	PRIMI	22.4	675	16.10.14	ALIVE	30.4.15						0	7	TLE	96	114	120		NVD		2.600			
79	228	jocelyn	24	PRIMI	23.5	492	21.10.14	ALIVE	30.4.15						0	9	TLE	104	95	107		NVD		2.800			
80	270	kumari	28	PRIMI	27.5	437	28.10.14	ALIVE	7.5.15						0	10	TLE	75	86	74		NVD		2.95			
81	339	stellamary	32	G3 P1L1A1	24.7	694	30.10.14	STILL BIRTH	11.5.15	yes		YES		yes	1	9.5	TLE	150			insulin	Lscs		3.5			85

82	407	muthamm al	30	PRIMI	22.3	784	2.11.14	ALIVE	11.5.15						0	7	ZLN	85	90	94		NVD		2.600			
83	493	lourdu	23	PRIMI	20.1	627	14.10.14	ALIVE	13.5.15						0	6	TLE	92	90	105		LSCS		3.9			
84	512	sylvia	26	G2A1	23.9	595	18.10.14	ALIVE	16.5.15						0	8.4	TLE	104	120	110		LSCS		3.6			
85	599	gomathy	22	PRIMI	22.6	613	12.10.14	ALIVE	18.5.15						0	7	TLE	104	90	86		NVD		2.75			
86	770	bharathi	25	PRIMI	26.3	800	29.9.14	ALIVE	21.5.15						0	8.5	TLE	88	82	80		LSCS		2.600			
87	938	anitha	23	PRIMI	23.8	720	13.10.14	ALIVE	25.5.15			YES			1	11	TLE	83	84	90		NVD		2.4			
88	1025	prema	25	G2A1	21.3	802	9.10.14	ALIVE	25.5.15						0	8.5	TLE	94	101	98		NVD	YES	1.5			
89	1172	selvamani	23	PRIMI	22.6	604	19.10.14	ALIVE	28.5.15						0	9	TLE	74	76	96		NVD		2.850			
90	1208	umasri	27	G2 P1L1	23.2	674	22.10.14	ALIVE	30.5.15						0	10.5	ZLN	80	92	110		NVD		2.9			
91	1397	kanchana mala	26	G2A1	22.4	591	26.10.14	ALIVE	31.5.15						0	9	TLE	110	98	104		LSCS		3.6			
92	1592	deviprabh a	29	G2 P1L1	23.1	404	25.10.14	ALIVE	1.6.15						0	10.5	TLE	102	110	105		LSCS		3.550			
93	1702	uma prabhu	22	PRIMI	25.2	1031	17.10.14	ALIVE	5.6.15						0	11	TLE	94	80	78		NVD		2.800			
94	1907	raji	29	G2P1L1	20.6	302	24.10.14	ALIVE	6.6.15						0	7	TLE	105	120	106		NVD		2.95			
95	1945	mala	22	PRIMI	22.5	681	28.10.14	ALIVE	12.6.15						0	9.5	TLE	84	78	90		NVD	YES	2.100			
96	2045	mary daniel	28	G2 P1L1	27.8	991	2.11.14	STILLBI RTH	15.6.15						0	9	TLE	180			INSULI N	LSCS		4.2			95
97	2432	karthika	25	PRIMI	24.8	745	12,11.14	ALIVE	19.6.15						0	11	ZLN	86	99	87		NVD		2.800			
98	2773	malathy	22	PRIMI	26.2	686	23.11.14	ALIVE	22.6.15						0	11.5	TLE	80	86	90		NVD		2.95			
99	2918	devi	29	G2 P1L1	25.9	635	21.11.14	ALIVE	25.6.15						0	10.5	TLE	94	105	110		LSCS		3.20			
10 0	3419	aruna	27	G3 P1L1A1	23.7	432	6.11.14	ALIVE	26.6.15						0	9.5	ZLN	102	94	115		LSCS		3.50			

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. S.Shwetha,
Postgraduate M.S.(Obstetrics and Gynaecology),
Madras Medical College,
Chennai – 600 003.

Dear Dr.S.Shwetha,

The Institutional Ethics Committee has considered your request and approved your study titled **"Incidence of gestational diabetes mellitus in HIV positive pregnant women on Antiretro Viral Therapy". No.29102014.**

The following members of Ethics Committee were present in the meeting held on 07.10.2014 conducted at Madras Medical College, Chennai-3.

1. Dr.C.Rajendran, M.D.,	: Chairperson
2. Dr.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.R.Nandhini, M.D., Inst.of Pharmacology, MMC	: Member
5. Prof.K.Ramadevi, Director i/c, Inst.of Biochemistry, MMC	: Member
6. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
7. Prof.S.G.Sivachidambaram, M.D., Director i/c, Inst.of Internal Medicine, MMC	: Member
8. Thiru S.Rameshkumar, Administrative Officer	: Lay Person
9. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
10. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLL
CHENNAI-600 003

INFORMATION SHEET

- Your specimen has been accepted.
- We are conducting a study to find the incidence of gestational diabetes milletes in pregnant women on anti retroviral therapy at institute of obstretics and gynecology egmore
- if found to have diabetes we may have to perform certain additional tests which in no way would be affecting your management or treatment
- The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator

Signature of participant

Date:

PATIENT CONSENT FORM

Title of the project:

Name : Date :

Age : IP No :

Sex : Project Patient No :

The details of the study have been provided to me in writing and explained to me in my own language.

I confirm that I have understood the above study and had the opportunity to ask questions.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected.

I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

I have been given an information sheet giving details of the study.

I fully consent to participate in the above study.

Signature

ஆராய்ச்சி தகவல் தாள்

தங்களது ரத்தம் பரிசோதனை இங்கு பெற்றுக்கொள்ளப்பட்டது

சென்னை அரசு மகப்பேரு மருத்துவமனை எழும்பூரில் சிகிக்கை பெற்று வரும் எச்.ஐ.வி நோயால் பாதிக்கப்பட்ட கற்பணி பெண்களில் சர்க்கரை நோயின் நிகழ்வு கண்டுபிடிக்க ஒரு ஆராயிச்சி நடைபெற்று வருகின்றது .

இரத்த பரிசோதனைக்கு பிறகு சர்க்கரை நோய் கண்டுபிடிக்கப்பட்டால் கூடுதல் பரிசோதனை செய்யப்படலாம் அது எந்த வகையிலும் நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிப்புக்கு ஏற்படாது என்பதை தெரிவித்துக்கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் போல் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம்

பங்கேற்பாளர் கையொப்பம்

தேதி

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு :

பெயர் : தேதி :

வயது : உள் நோயாளி எண் :

பால் : ஆராய்ச்சி சேர்க்கை எண்

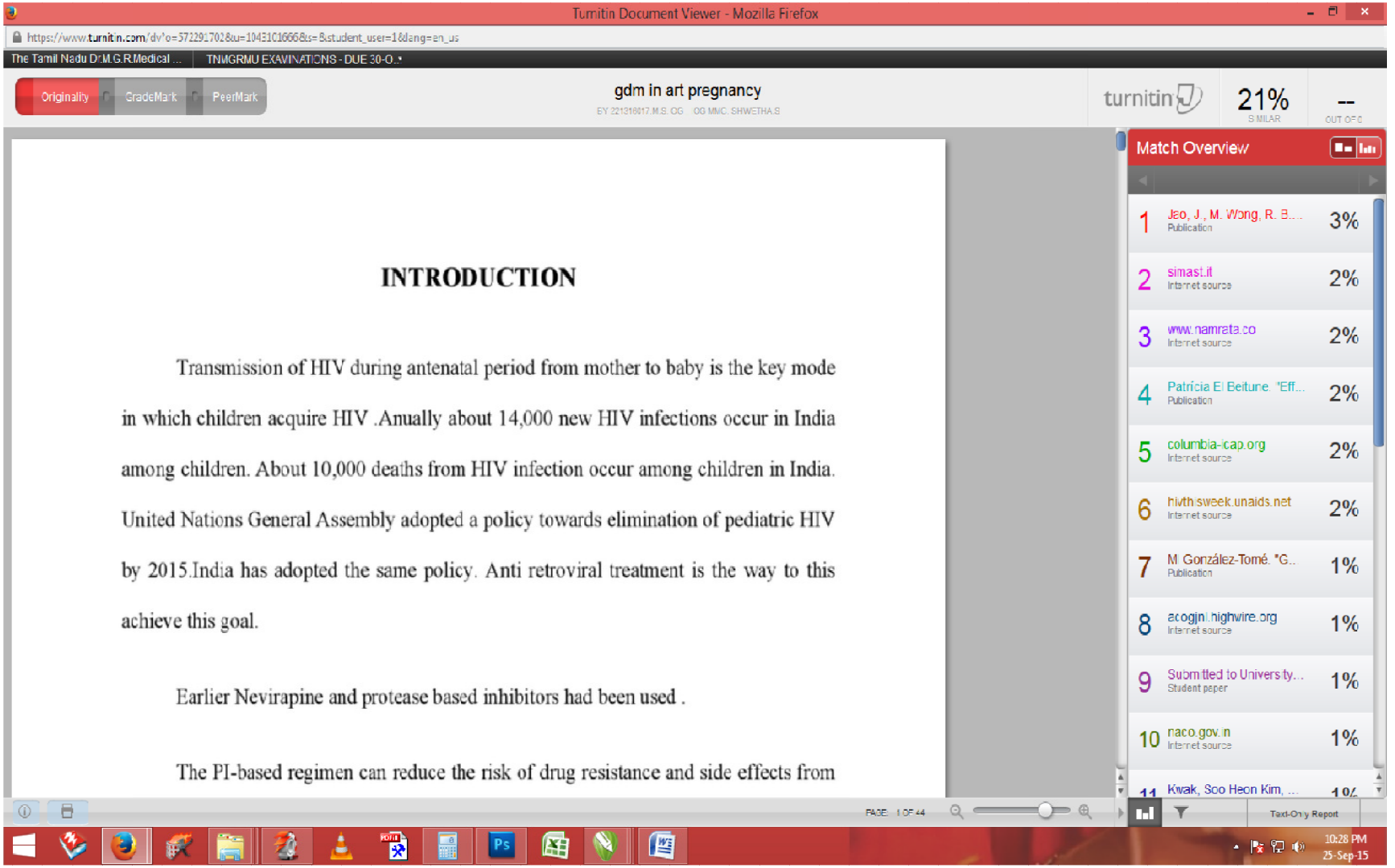
எனக்கு ஏச்.ஐ.வி. நோய் இருப்பதால் நான் கர்பணியாக இருக்கும் போழுது அதற்குண்டான சிகிச்சை எடுத்துக்கொண்டால் தான் என் குழந்தையை பாதிக்காமல் காப்பாற்ற முடியும் என்பதை நான் அறிந்துகொண்டேன். அத்துடன் சிகிச்சையில் பொழுது சில மருந்துகளால் சர்க்கரை நோய் ஏற்பட வாய்ப்புள்ளது என்பதையும் நான் அறிந்து கொண்டேன். அதற்குண்டான இரத்த பரிசோதனை செய்து கொண்டு தக்கசிகிச்சை பெற்றுக்கொள்ள எனக்கு முழு சம்மதம்

இந்த ஆராய்ச்சியில் பிறரின் நிர்ப்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் தான் பங்கு பெறுகிறேன். மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்து கொண்டென்.

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு நான் எனது சம்மந்தத்தைத் தெரிவிக்கிறேன்.

கையொப்பம்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Earlier Nevirapine and protease based inhibitors had been used .
The PI-based regimen can reduce the risk of drug resistance and side effects from
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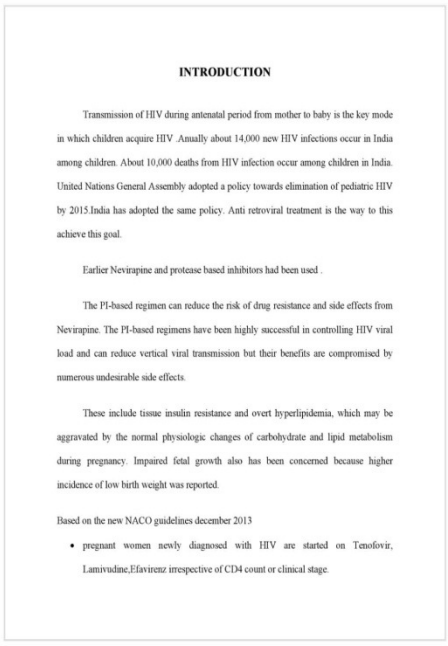

INTRODUCTION

Transmission of HIV during antenatal period from mother to baby is the key mode in which children acquire HIV .Anually about 14,000 new HIV infections occur in India among children. About 10,000 deaths from HIV infection occur among children in India. United Nations General Assembly adopted a policy towards elimination of pediatric HIV by 2015.India has adopted the same policy. Anti retroviral treatment is the way to this achieve this goal.

Earlier Nevirapine and protease based inhibitors had been used .

The PI-based regimen can reduce the risk of drug resistance and side effects from Nevirapine. The PI-based regimens have been highly successful in controlling HIV viral load and can reduce vertical viral transmission but their benefits are compromised by numerous undesirable side effects.

These include tissue insulin resistance and overt hyperlipidemia, which may be aggravated by the normal physiologic changes of carbohydrate and lipid metabolism during pregnancy. Impaired fetal growth also has been concerned because higher incidence of low birth weight was reported.

Based on the new NACO guidelines december 2013

- pregnant women newly diagnosed with HIV are started on Tenofovir, Lamivudine,Efavirenz irrespective of CD4 count or clinical stage.