Association between Hormonal Contraceptive Use and Glycemic Severity in women suffering from Gestational Diabetes Mellitus in Bangladesh.

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Abstract

Background: Gestational Diabetes mellitus is the type of diabetes that is first diagnosed at pregnancy; which can progress into Diabetes Mellitus type 2 after pregnancy. GDM has the capability to have harmful effects both on mother and the child. The prevalence is increasing worldwide with Bangladesh being a country of higher prevalence. Bangladesh is also having an increasing prevalence of contraceptive use. Hormonal contraceptives are widely used and contain progestin which exerts androgenic effect that might alter carbohydrate metabolism, thus opening a possibility to develop GDM and poor glycemic control in users.

Objectives: To estimate the proportion of hormonal contraceptive users and non-users among GDM mothers and observe the glycemic level in women with GDM in relation to Hormonal Contraceptive use.

Method: A quantitative study designed as retrospective and observational was conducted in BIRDEM-2 hospital, Dhaka from 7th December 2014 to 23rd February 2015. Data on hormonal contraceptives and other necessary variables was collected with structured questionnaire from 249 pregnant women with GDM.

Result: Out of 249 participants with GDM, 111(44.6%) were hormonal contraceptive users and 138(55.4%) were non-users. Hemoglobin level was significantly lower and ABF level was significantly higher among the users. Marked glycemic severity was noticed among the participants with positive family history of DM type 2 (P= 0.02).

Conclusion: According to the findings, hormonal contraceptive- particularly combined oral contraceptive low dose has no role in developing GDM or alter glycemic control among the users. However, participants with family history of DM type 2 have higher chance of suffering from glycemic severity.

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ABBREVIATIONS (in alphabetical order)

ABF: After Breakfast Blood Glucose

ADA: American Diabetic Association

BGMEA: Bangladesh Garment Manufactures & Exporters Association

BIRDEM: Bangladesh Institute for Research in Diabetes, Endocrine and Metabolic Disorders

BMI: Body Mass Index

COC: Combined oral Contraceptive pill

DBP: Diastolic Blood Pressure

DM: Diabetes Mellitus

ECP: Emergency Contraceptive pill

FAO: The Food and Agriculture Organization of the United Nations

FAOSTAT: The Food and Agriculture Organization Corporate Statistical Database

FBG: Fasting Blood Glucose

GAVI: Global Alliance for Vaccines and Immunization

GDM: Gestational Diabetes Mellitus

IDF: International Diabetic Federation

NGO: Non-governmental Organization

POP: Progesterone only pill

SBP: Systolic Blood Pressure

UNICEF: United Nations International Children's Emergency Fund

WHO: World Health Organization

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. This is a disease which threatens severe morbidity to both the mother and the fetus. Also, sudden Intra-uterine death of the fetus in otherwise normal condition is considered a grave consequence of GDM. Furthermore, 50% of the GDM mothers develop type 2 diabetes after the birth of the child [1].

The prevalence of GDM has been alarmingly increasing. According to International Diabetes Federation (IDF), 1 in 25 pregnancies are affected by GDM worldwide [2].

Along with other adversities, the ability of hormonal contraceptive to affect glycemic status has been considered and researched. One study by Berenson et al. suggests that the use of Injectable contraceptive slightly increases the fasting blood sugar level and insulin levels [3].

The known risk factors of Gestational Diabetes Mellitus are considered to be age, parity, BMI and family history of GDM and DM. Apart from these known factors, a study by Kramer et al. showed that women who used hormonal methods of birth control had higher odds (40%) for GDM than did women who used non–hormonal contraception [4]. However, to the best of my knowledge, no study related with hormonal contraceptives has yet been done on South-Asian population who are genetically predisposed to develop diabetes in earlier age [5].

Bangladesh has an increasing prevalence of hormonal contraceptive use, which stands at 61% and also the increasing prevalence of GDM that was 9.7% in 2013 [6]. Whether the use of hormonal contraceptive is attributing to the increased prevalence of GDM has not been considered yet. The population at risk could benefit from researches regarding this issue. In addition, the effect of hormonal contraceptive on glycemic status of GDM mothers needs be studied as well.

This study has been conducted on participants with GDM to investigate the status of glycemic severity among the users and non-users. In addition, the use of hormonal contraceptive in relation to demographic characteristics among them is also observed.

BACKGROUND OF THE STUDY

i. COUNTRY PROFILE: BANGLADESH

Geographical Location:

Bangladesh, officially known as 'Peoples Republic of Bangladesh' is a country of 147,570 square kilometer and is situated in South Asia. Bangladesh is bordered by India to its West and North. To the East, Bangladesh is bordered by India and a strip of Myanmar. To the South, the country faces the Bay of Bengal. Terrain of Bangladesh is mostly flat with some hilly areas in south east. Bangladesh also possesses the unique name tag of 'The land of rivers' because of its abundance of rivers as the country is dominated by the largest delta of the world – Bengal Delta.

Climate of the country is sub-tropical monsoon. Average temperature of winter remains within 11 to 20 degree Celsius (October to February). In summer, it is 21 to 38 degree Celsius (March to September).

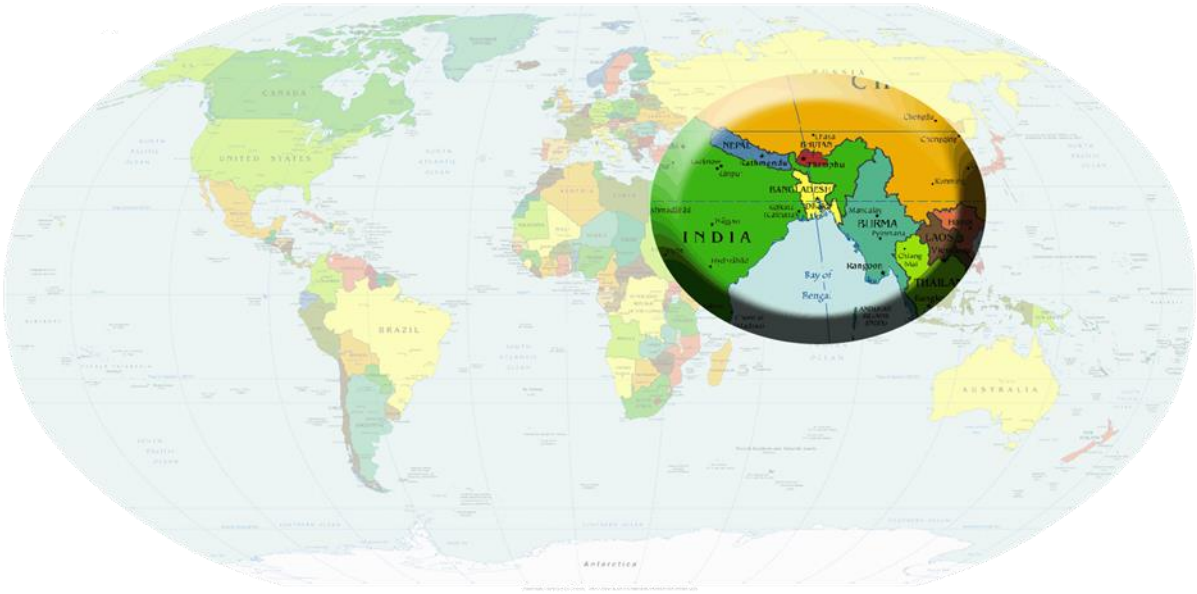

Figure 1: Bangladesh in World Map

History of Birth:

Bangladesh has been a part of British India until the partition in 1947 from which two countries -India and Pakistan emerged. Though sharing no borders, Bangladesh was tied to Pakistan due to the religion based division. Bangladesh became a sovereign country in 1971.

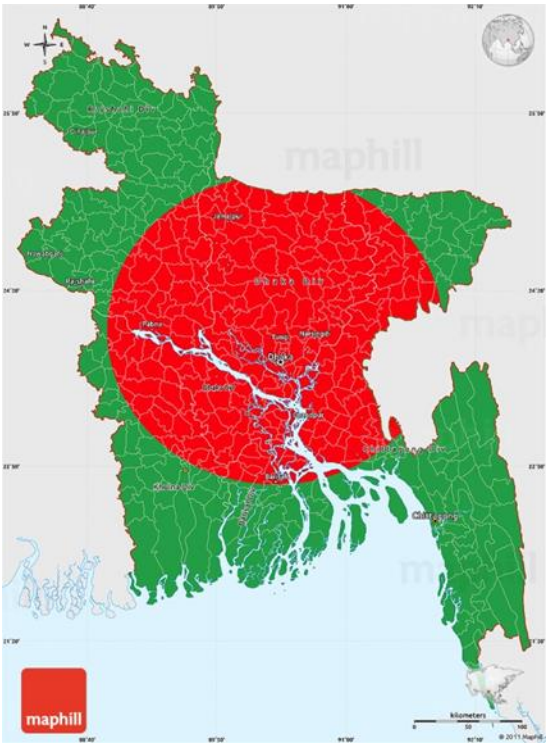

Figure 2: Map of Bangladesh

Figure 3: Flag of Bangladesh

Flag of Bangladesh:

The flag of Bangladesh consists of a red disc on top of a green field. Red disc symbolizes the rising sun and the blood of the martyrs of independence. The green field depicts the lushness of the country. Source: National Encyclopedia of Bangladesh.

Cities:

Dhaka is the capital and the largest city. It is situated in central Bangladesh, on the banks of river Buriganga. Dhaka has been the destination of ongoing migration from rural areas and other cities and towns. Due to the lack of decentralization, Dhaka remains the most important and convenient city for treatment, education and business and employment with best institutes and best options. Dhaka population is accounted as 15 million in 2013. According to Far Eastern Economic Review, by the year 2025 Dhaka will be home to 25 million people.

Situated in the southeastern part of the country, Chittagong is the main sea port and second largest city of Bangladesh. Rajshahi, Sylhet, Khulna, Rangpur and Barisal are some of the other important cities.

Population:

People of Bangladesh are known as 'Bangladeshi'.

According to the 2011 census report, which is the latest prepared by the Bangladesh Bureau of Statistics [7], the total Population is 158,073,526. However, a July 2014 report from the World Fact Book [8] has a revised figure of 166,280,712.

With a birth rate estimated at 25.12 births/1,000 people and a death rate of 8.47 deaths/1,000 people, the population of Bangladesh is growing at a rate of 1.59%.

<u>Age Structure:</u>

0-14 years: 33.8% (male 23,069,242; female 21,995,457)

15-64 years: 62.8% (male 42,924,778; female 40,873,077)

65 years and over: 3.4% (male 2,444,314; female 2,069,816)

Sex Ratio (males per 100 females): 100.3

86.6% population is Muslims, 12.1% are Hindus; 0.6% is Buddhists and 0.4% is Christians in Bangladesh. People of all religions live side by side in socio-cultural harmony and peace.

98% of the population are ethnically Bengali and speaks the official language Bangla. Minorities include indigenous people from Chittagong hill tracts and some northern parts of Bangladesh. The country's social and cultural norms share large similarity to those found in Indian and Pakistan. Source: Bangladesh National Web Portal [9]

Economy:

Bangladesh is a developing country and is among the low-income country group. It is looking forward to become one of the middle-income country groups by 2021.Despite the continuous political conflict; the economy of Bangladesh has increased roughly 6% every year since 2004.

GDP: US$ 1044 (per capita in2013)

Poverty level: 25% (within US $ 2)

Foreign Grant Dependency: 2%

78% of export earnings come from the textile industry, as Bangladesh is the world's fourth largest textile exporter. Remittances from the Bangladeshi diaspora and overseas workers provide vital foreign exchange earnings, accounting for US$14 billion in FY 2013-14. Bangladesh is also a major agricultural producer, particularly in the global production of rice (4th), fisheries (5th), and jute (2nd).

Source: Bangladesh National Web Portal [9], BGMEA [10] and FAOSTAT [11]

Education:

According to UNICEF, Literacy Rate in Bangladesh is: 57.7% and Female Literacy Rate: 53.4% [15]

Public schools and Colleges and Universities of Bangladesh are run and hugely subsidized by the Government. As a sincere step towards expanding female literacy, education for girls up to higher secondary level is free. In addition to that, stipend and food grains are offered to school going children in order to reduce child labor and improve school attendance. In recent years, school books are given to school children for free on the first day of school session.

Along with public institutions, there are private institutions running all over the country which make it feasible that each and every child can get a chance to be educated according to its parents afford. In addition, free education is provided through numerous schools run by NGOs (Non-Governmental Organizations) in all parts of the country.

Nevertheless, without the effort of UNICEF and various NGOs, the achievement in education sector would not have been possible.

The educational system of Bangladesh is categorized as:

Primary Level..... Up to 5 years

Secondary Level ..... 6-10 years

Higher Secondary level ..... 11-12 years

Graduation (Honors)..... 13-16 years or more

Post-graduation .....17/18 years or more

Gender Inequality:

In 2013, Bangladesh was ranked 142 out of 187 countries on the Human Development Index and 115 out 149 countries on the Gender Inequality Index.

Though strategies on women empowerment have been implemented in order to close the gender gap, Bangladeshi women still faces the threat of sexual harassment, rape, domestic abuse and acid violence. Despite the gender discrimination, women are working in every sector and playing the principal role in health promotions in rural areas and also in school teaching. Women are being encouraged to become entrepreneurs and many successful ventures are already established.

80% (around 2.8 million) of employees in ready-made garment industry are female [10].

In February 2015, at a seminar, Noble Laureate Amartya Sen said –

"India can learn from Bangladesh on its success in gender equity,"

However Bangladesh still has to go a long way to create a safer and more encouraging environment for women.

Overall Health Status:

Life expectancy at Birth: 70.3 years (2012)

Infant Mortality Rate: 33 deaths/1,000 live births. (2012)

Under Five Mortality Rate: 41 deaths/1,000 live births. (2012)

According to Bangladesh Health Profile of WHO, communicable diseases accounts for 45% and non-communicable diseases accounts for 43% of the 'years of life lost' in Bangladeshi adults.

Along with many low and middle income countries, Bangladesh is facing the double burden of disease. The country has been experiencing an epidemiological transition from communicable disease to non-communicable diseases. Diseases like Diabetes Mellitus and Cardio-vascular diseases and Carcinomas are becoming epidemic and causing morbidity and mortality in large

scale with bigger impacts on socio-economic factors. Beside them long standing communicable diseases like diarrhea and tuberculosis are also still present [12]

Malnutrition stands as a root cause of several diseases which can lead to morbidity and mortality as well. The consequences of Malnutrition does not only affect the individual but can be passed on to the next generation as malnourished mothers gives birth to children who struggle to develop and thrive. Girl children born to these mothers grow up to become malnourished mothers themselves and thus the vicious cycle continues.

The National Nutrition Programme which is run by the government covers approximately 20% of the population only. Fortunately UNICEF has an intense nutrition improvement programme across the country which targets the lifecycle from infancy to childbearing years.

The proportion of underweight children dropped to 36% in 2011 from 43% in 2004 [13]

Immunization:

Immunization has been a successful endeavor of Bangladesh. The government provides immunization through Expanded Program on Immunization in Bangladesh. With the patronization from WHO (World Health Organization) and GAVI (Global Alliance for Vaccine and Immunization), immunization is provided as Essential Service Delivery and is made available to mass population through governmental and non-governmental organization. The coverage reaches target population of both urban and rural areas.

Currently children are immunized against TB, Polio, Diphtheria, Pertussis, Tetanus, Hepatitis B, Measles, Haemophilus influenza type b and Night Blindness. Immunization for Tetanus is offered to the women of reproductive age.

Sources: WHO [14], UNICEF [15] and Bangladesh demographic and health survey 2011[16].

Health care system:

The health care system of Bangladesh comprises of both the public and the private institutes. The public system follows the local government system. Bangladesh is divided in 7 divisions, comprising of 64 districts, 488 upazillas and 4550 unions. Along with several tertiary level teaching hospitals in every division heads, there are secondary level hospitals in districts and primary health care centres in all upazillas. However, the health system heavily depends upon the private and NGO run institutes. Private institutes comprise all primary, secondary and tertiary level hospital whereas NGOs mostly comprises primary care and some secondary care centers. Particularly for Nutritional and Family Planning promotions in rural areas, NGOs play the key role.

Although the epidemic of Non-Communicable Diseases now persists for more than a decade, not much governmental approach has been noticed; also not focused adequately by other organizations. Till date, Diabetic Association of Bangladesh is the only major organization to address and challenge the issue of Non-Communicable Disease.

Millennium Development Goal:

Bangladesh has already achieved extra-ordinary success in several targets of MDGs. Reducing poverty gap ratio, attaining gender parity at primary and secondary education, under-five mortality rate reduction , containing HIV infection with access to antiretroviral drugs, children under five sleeping under insecticide treated bed nets, detection and cure rate of TB under DOTs are the fields where improvement is seen [17]. The target of reducing Maternal Mortality Rate to 143/100,000 is expected to be met in 2015; which has been 170/100,000 in 2014 according to World Bank survey.

Maternal Health:

Maternal Mortality Rate is recorded as 170 deaths/100,000 live births according to World Bank survey in 2014 [18]

Mean age of the mothers' at the birth of the first child was 18.1 in 2011. The total fertility rate accounted for 2.45 children born/woman.

The current contraceptive prevalence of 61.2 % has contributed to the benefit of less fertility rate, thus lowering the population growth rate.

Antenatal care:

54.6 % women visit health care facility for antenatal checkup at least once in pregnancy. Only 25.5% women make it up to four visits.

Delivery care:

31.7% of deliveries are attended by skilled attendant in Bangladesh. Here, skilled attendants include doctors, nurses and midwives.

Only 28.8% deliveries take place in medical facilities leaving 71.2% as home deliveries.

The prevalence of caesarian section is 17.1%

Anemia in Pregnancy: Due to malnutrition, anemia in pregnancy is a common problem in Bangladesh.

[Sources: 7, 8, 9, 13, 18]

ii. DIABETES MELLITUS

The term 'diabetes mellitus' describes a metabolic disorder of multiple aetiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long–term damage, dysfunction and failure of various organs (WHO 1999) [19].

Types of Diabetes Mellitus:

There are three main types of diabetes:

1. Type 1 or Insulin Dependent Diabetes Mellitus
2. Type 2 or Non-Insulin Dependent Diabetes Mellitus
3. Gestational Diabetes Mellitus

Diabetes Mellitus type 1:

Type 1 diabetes is also called juvenile-onset diabetes. It is usually caused by an auto-immune reaction where the body's defense system attacks the cells that produce insulin. People with this form of diabetes need injections of insulin every day in order to control the levels of glucose in their blood.

Diabetes Mellitus type 2:

Type 2 diabetes is also called non-insulin dependent diabetes or adult-onset diabetes, and accounts for at least 90% of all cases of diabetes. It is characterized by insulin resistance and relative insulin deficiency, either or both of which may be present at the time diabetes is diagnosed. Type 2 diabetes may remain undetected for many years and the diagnosis is often made when a complication appears or a routine blood or urine glucose test is done

Gestational Diabetes Mellitus:

Gestational Diabetes Mellitus is the third type, which is the main of concern in this study. It is the diabetes diagnosed in pregnancy. Insulin is needed in most of the cases to control blood sugar level.

Complications of Diabetes Mellitus:

Complications of Diabetes are divided into microvascular (due to damage to small blood vessels) and macrovascular (due to damage to larger blood vessels). Microvascular complications include retinopathy (damage to eyes leading to blindness), nephropathy (damage to kidneys leading to renal failure) and neuropathy (damage to nerves which can lead to impotence and diabetic foot disorder, with further threat to amputation of limb)

Macrovascular complications include cardiovascular diseases such as heart attacks, strokes and insufficiency in blood flow to legs [20].

Global Burden of Diabetes Mellitus:

In 2014 the global prevalence of diabetes was estimated to be 9% among adults and an estimated 4.9 million deaths were directly caused by diabetes in the same year.

More than 80% of diabetes deaths occur in low- and middle-income countries.

WHO predicts that diabetes will be the 7th leading cause of death in 2030.

A matter of serious concern is that 46.3% of diabetes remains undiagnosed.

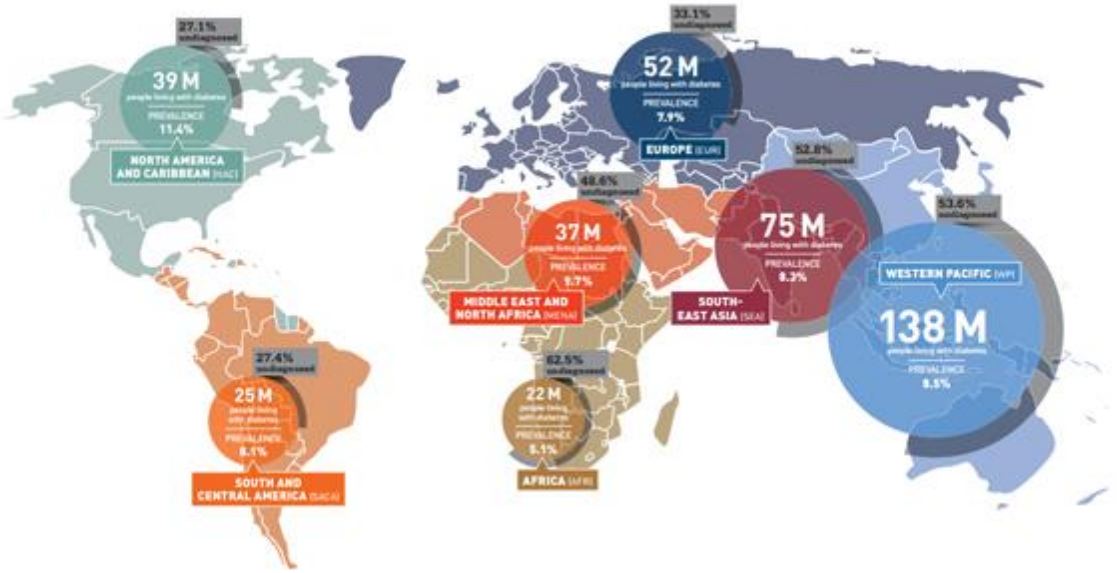

Figure 4: World prevalence of Diabetes Mellitus (by IDF)

Diabetes Mellitus in Bangladesh:

In 2011, Bangladesh had 8.4 million people with Diabetes, which is almost 10% of the population. Prevalence of diabetes among adults had increased substantially. From 1995 to 2000 it was 4%, and then from 2001 to 2005 it became 5%. Within 2006 to 2010, it became 9%. According to the International Diabetes Federation; the prevalence will be 13% by 2030.

Bangladesh in 2014: According to International Diabetes Federation (IDF),

Number of deaths in adults due to diabetes was 111,371.

Prevalence of diabetes in adults (20-79 years) stands at 6.3 %

Cost per person with diabetes (USD) accounted for 42.6 per year.

iii. GESTATIONAL DIABETES MELLITUS

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [1]. It develops in one in 25 pregnancies worldwide and is associated with complications to both mother and baby. GDM can adversely impact both mother and the fetus. The consequences are not limited to during or after pregnancy, but also later in life. According to International Diabetes Federation, approximately half of women with GDM develop type 2 diabetes within five to ten years after delivery. A study by Dabelea et al. suggested that among the offspring, intra-uterine exposure to diabetes conveys higher risk for obesity and Diabetes Mellitus type 2 [21]. Other similar studies also came up with similar results.

Effect of GDM:

Studies have revealed that compared to non-GDM group, pre-eclampsia, urinary tract infection, puerperal sepsis and surgical intervention are more common in GDM group of Bangladeshi women. Also, congenital anomaly, pre-term birth, low birth weight, macrosomia, respiratory distress syndrome, neonatal jaundice and perinatal mortality are more prevalent in neonates of GDM group [22].

Known Risk factors of GDM:

Age, obesity, personal history of GDM, family history of diabetes are the known risk factors.

Prevalence of GDM:

The world prevalence varies from 1% to 16% according to the population and the diagnostic criteria used [8].

In Bangladesh, the latest prevalence ranged from 9.7% (WHO criteria, 2013) to 12.9% (ADA criteria, 2013) was 9.7% (WHO criteria) or 12.9% (ADA criteria) in 2013.

It was 7.5 %(urban) and 13.2 %(rural) in 2012; 8.2% in 2005 (rural, WHO criteria). [6,22,23,24].

iv. HORMONAL CONTRACEPTIVES

As the concept of family planning and birth control has been able to reach almost every corner of the world, the usages of hormonal contraceptives are becoming more prevalent. Although it can be counted as a blessing to the world, hormonal contraceptives are not without side-effects. The common adverse effects can range from spotting, weight gain, cardiovascular risk, thromboembolism, migraine, mood change to subfertility. The injections and Implants are believed to have stronger affect because they contain much more hormone than the oral pills. Oral pills are also available in various hormonal doses. In spite of being considered safer, the low dose pills are also capable of initiating side effect in an individual has been suggested by a study by Sabatini et al. [25].

Contraceptives in Bangladesh:

Though Bangladesh is still conservative in many social issues, significant progress has been noted in family planning and contraceptive use. While the prevalence rate of Contraceptive use was only 8% in 1975, it leaped to 61% in 2011 among married women aged 15-49 years.

Oral contraceptive pill is the most widely used method (27%), followed by Injectable (11%) and Implant (1%).

Source: Bangladesh Demographic and Health Survey 2011 [16] & Partners in Population and Development [26].

The types of pills available are- Combined Oral Contraceptive pills (low dose), Progesterone only pills and Emergency Contraceptive pills.

The most popular among the pills are the Low dose Combined Oral Contraceptive Pills. The composition is basically estrogen and progestogen used in various synthetic formulation and dosage. For example, Femicon contains 0.30 mg Norgestrel BP and 0.03 mg Ethinyl Estradiol and Nordett-28 contains 0.15 mg of levonorgestrel and 0.03 mg of ethinyl estradiol. Both are low dose combined oral contraceptive pills.

Femicon, Shukhi, Nordett-28 are the widely used because of their attractive advertisements, availability and affordability.

Figure 5: Packages of Nordette-28 and Femicon (Low dose Combined Oral Contraceptive Pills)

Two types of Injectable are available in Bangladesh. They are - Depot medroxy progesterone acetate (DMPA) and Norethisterone enanthate.

SOMA-JECT is a brand name of DMPA available in the market and contains 150 mg DMPA in one vial.

Only one type of Implant is available- Etonogestrel. Brand name of it is Implanon and it contains 68 mg of etonogestrel.

Bangladesh has been a chosen country for clinical trials of Injectable and Implant hormonal contraceptives since 1980s. There have been many controversies because of improper information to the users and violating human rights. Depo-provera(DMPA), Noristerat (Norethisterone enanthate) and Norplant has been in wide use in Bangladesh with much controversies because of their side effects [38,39,40].

Injectable and Implant Contraceptive are administered once in three months and are cheaper. They are more commonly used in rural areas. However, Oral pills are most popular as they can

be obtained over the counter from any pharmacy and are affordable too. Women of Bangladesh largely use oral pills on the basis of advertisement and peer advices. Consulting a physician for birth control has not been a common concept in Bangladesh.

v. Pathophysiology between Hormonal Contraceptive and GDM

All types of Hormonal Contraceptives contain Progestin as a potent component. Progestin is a synthetic progestogen which exerts similar effect of progesterone.

Administration of Progestin prevents ovulation by controlling the surge of Luteinizing hormone in a menstrual cycle and thus prevents conception. The adverse effect of it includes possibility to impair glucose tolerance and increase insulin resistance. Blood sugar may rise and Diabetes may be precipitated by long term use. (Textbook of Pharmacology by S.D. Seth. 3rd edition. Page 71) [27]

Progestin exerts androgenic effect which can manifest metabolically causing glucose intolerance; as well as enhancing weight gain as a symptom [28].It is possible that during pregnancy, lingering effect of the progestin combined with metabolic stress induced by placental hormone effects carbohydrate metabolism. Thus it threatens the vulnerability of developing Gestational Diabetes Mellitus and poor glycemic control.

vi. Literature Review

Although the role of hormonal contraceptives on glycemic status in pregnancy has been a topic of debate and confusion, not much research has been done on this issue. Various studies in different population have been conducted to investigate the risk factors of GDM. Unfortunately the relation with hormonal contraceptive and glycemic severity has not been considered much. After searching databases of PubMed, Google Scholar, BioMed Central, IMSEAR (Index medicus of South East Asian Region) and Bangladesh Journal Online, only a couple of articles are found regarding this specific indication.

One of them is 'Association between Contraceptive Use and Gestational Diabetes: Missouri Pregnancy Risk Assessment Monitoring System, 2007–2008' by Kramer et al. [4]. This American study showed that Women who used hormonal contraceptives had higher odds for gestational diabetes (adjusted odds ratio [AOR] = 1.43; 95% confidence interval [CI], 1.32–1.55) than non-hormonal contraceptive users. Another study is 'Androgenicity of Progestins in Hormonal Contraceptives and the Risk of Gestational Diabetes Mellitus' by Hedderson et al. This study was conducted in a multi-ethnic group of women in U.S.A. The result suggests that high-androgenic hormonal contraceptive increases the risk of GDM modestly (OR 1.43) [29]. Another study was conducted in the Philippines on 'Prevalence and Risk Factors of Gestational Diabetes Mellitus at the University of Santo Tomas Hospital' by Lim-Uy SW, et al. Along with several other risk factors, it claims that risk of GDM was strongly associated with use of hormonal contraceptive (OR 8.48) [30].

On account of hyperglycemia, a study by Berenson et al. showed that the use of injectable hormonal contraceptive (DMPA) can lead to slightly higher fasting glucose and insulin, but low dose oral contraceptive does not have this effect [3]. Another study suggested no major difference in carbohydrate metabolism between different hormonal contraceptives in women without diabetes [31]

Studies on carbohydrate metabolism [3 & 31] were done on non-pregnant, non-diabetic women.

vii. Statement of Problem

In a study of ethnical prevalence of Gestational Diabetes Mellitus, the result projected that the overall prevalence of GDM was 6.7 % (CI 6.0 %–7.4 %). In Indian population it was 16.7 %. In comparison, the prevalence in other ethnicities are as follow - Anglo-Celtic women 3.0 %, Chinese 15.0 %, Vietnamese 9.6 %, Arabic 7.3%. [32].The highest prevalence is among the Indian ethnicity which is also same as South-Asian Ethnicity.

Due to South-Asian Ethnicity, Bangladeshi population faces a much greater risk of developing Diabetes Mellitus at early age. According to a study by Hunsberger et al., especially Asian women with both normal and high BMI possess increased risk of GDM [33]. Because of the phenotype, Bangladeshi females are born as a small, low lean mass baby. Later in life they are prone to develop central obesity for the unique fat deposition pattern which leads to metabolic syndrome. As a consequence, they develop diabetes early. Included to the particular phenotype and fat deposition pattern, there are low physical activity and carbohydrate-fat dependent dietary pattern of the Indian-Asians. Moreover there is the possibility of pancreatic βcell dysfunction because of fewer numbers of β cells at birth due to fetal starvation [34]. These ethnic attributions are believed to play a role on developing Diabetes type 2 and Gestational Diabetes Mellitus. Along with these, controlling the glycemic severity becomes more difficult.

Over time, Bangladeshi women have accepted contraceptive use extremely liberally. Majority population is Muslim in Bangladesh and contraceptive has not been considered a religious taboo there. With uprising economy and local production of medications, the ability to afford hormonal contraceptive pills is becoming common also. In recent years, the increasing prevalence in both Contraceptive usage and GDM has become noticeable. A correlation between these two factors, whether the pathophysiology of hormonal contraceptive is playing a role in GDM considers investigation to be done. Result of which might be able to lead a way for further research and future implications.

This calls for a study to be done in Bangladesh to estimate the relationship of Hormonal Contraceptive and Gestational Diabetes in Bangladeshi women.

vii. Justification of the study

Bangladesh can be considered among the countries with higher prevalence of GDM. With all the established risk factors of GDM being non-modifiable (age, ethnicity, obesity, family history of diabetes), only a few modifiable factors are left to control and decrease the prevalence rate. Hormonal Contraceptive use could be a modifiable factor if any association is proved. Better control of blood sugar level can also be achieved which will deter complications of hyperglycemia. Also, as half of the GDM mothers develop Type 2 DM as a sequel, decreasing GDM prevalence would decrease the DM prevalence as well. Whether GDM and glycemic severity is being influenced by Hormonal Contraceptives usage needs to be investigated for further implications.

Research Question

Is glycemic severity more in GDM patients who used hormonal contraceptive?

Is GDM more common among the users of hormonal contraceptives in Bangladeshi women? What are the characteristics of the Hormonal Contraceptive users?

Objective

1. To estimate the proportion of Gestational Diabetes Mellitus among Hormonal Contraceptive users and Non-users.

2. To observe the glycemic level in women with GDM in relation to Hormonal Contraceptive use.

Hypothesis

GDM is more common among the hormonal contraceptive users and the users have poor glycemic control.

MATERIALS and METHODOLOGY

i. Population, Design and Location of the study

Target population:

The target population of this study is the pregnant women who are suffering from Gestational diabetes Mellitus in Bangladesh.

Study population:

Study population has been specified as the pregnant women with GDM who attended the Obstetrics out-patient department for antenatal check-up in BIRDEM-2.

Study design:

A retrospective study was designed to collect data for this research. The study was quantitative and observational.

Study Location:

This study was conducted in Dhaka, the capital of Bangladesh. The hospital selected for the study is a tertiary level hospital specialized in Diabetes and is located in a populated area of South Dhaka which is well connected by public transport from any corner the city.

Study hospital:

Mohila and Shishu Diabetes Endocrine and Metabolic Hospital, BIRDEM-2.

Segun Bagicha, Dhaka.

ii. BIRDEM-2

Bangladesh Institute of Research & Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) is a tertiary level hospital situated in Dhaka. It is the central institute of Diabetic Association of Bangladesh (BADAS). The unique program of BADAS is to deliver a comprehensive health care to a vast number of diabetic populations all over Bangladesh.

Dr. Mohammed Ibrahim founded BADAS and started BIRDEM as an outpatient facility for diabetic care in 1956. He was the first one to thought about diabetic care in Bangladesh.

The motto of Dr. Ibrahim `no diabetic patients should die untreated, unfed or unemployed even if she/he is poor'.

Starting as an outpatient department, BIRDEM has now become an enormous institution comprising two hospitals. BIRDEM, the initial and central institute comprises of medicine and surgical departments and BIRDEM-2 runs the Gynecology-Obstetrics and Pediatrics departments.

As BIRDEM is the only hospital to have specialized care system for diabetes, a huge number of patients from every corner of the country is treated here. Patients with diabetic complication from other tertiary level hospitals from the city are also referred to BIRDEM. Registered Diabetic patients receive treatment at a subsidized rate and patients who Patients who cannot meet treatment costs receive help from the social welfare services of BIRDEM.

BIRDEM-2 is located at Segun Bagicha, a populated area of the Dhaka city and it is also the original location of BADAS. The services here are exclusively for women and children. It has initially started with 118 beds in 2012 with a plan to expand further.

On average, 3 to 4 deliveries take place daily at BIRDEM-2. The patients are mostly with pre-gestational diabetes and GDM. Many cases of confirmed GDM or suspected GDM are referred to this hospital for optimum care of diabetes. If a diagnostic report confirming GDM is not available from a trusted laboratory, patients are screened again. After confirmation they are registered and their demographic, medical, clinical, family history are recorded. A book is issued

where all necessary information along with lab results are noted. From then on, this book is used for prescriptions, advices, and discharge notes, which becomes a comprehensive treatment history book.

In the month of December 2014, a total of 1928 patient attended the outpatient department of Gynecology and Obstetrics. Among them, 1033 were Diabetes Mellitus (type 1 and 2), 490 had Gestational Diabetes Mellitus and 399 were Non-Diabetic. (source: BIRDEM administration).

iii. Research Instruments:

Structured Questionnaire (Appendix-1).

Sources for data were,

a) Answers from the participants in interview

b). Antenatal cards

c). Diabetic book of the patient with GDM (if available)

iv. Inclusion and Exclusion Criterion

Inclusion Criteria:

a. Pregnant women diagnosed with GDM within 24 to 28 gestational weeks

b. If contraceptive user, history of Hormonal Contraceptive use at least 2 years before pregnancy

c. With single pregnancy

d. Those who were willing to take part in the study with informed consent.

Exclusion Criteria:

a. Those that are diagnosed with Diabetes Mellitus Type 1 or Type 2

b. Those that refuse to participate in the study.

c. Those who did not look physically well enough to take part in the study.

v. Sample Size:

Assuming 20% of non-contraceptive users have GDM; the sample size required for a population proportion of 20% with a precision of 5% and a 95% CI is 246.

On field, data was collected from 249 patients.

Sampling procedure:

Sampling was done as continuous sampling in the outpatient department of BIRDEM-2.

Data was collected from 249 patients who fulfilled the inclusion criteria and agreed to participate.

vi. Pilot study:

A pilot study had been conducted prior to the initiation of the principal study. The pilot study was done on 5 participants to identify the potential problems in the collection of data. Necessary adjustments were made in the questionnaire as required.

vii. Data collection procedure:

In BIRDEM-2, the Gynecology and Obstetrics department is divided into 4 Units. Each unit has a fixed day of the week for outpatient services and a patient receives treatment throughout the pregnancy under the same unit in which she was booked in her first visit. Obstetrics check-up is done in room 216 and check-up for diabetes is done in an adjacent room, room 217.

In room number 217, diabetic patients with pregnancy take their serial by submitting their diabetic book if registered or prescriptions and reports if unregistered. Patients were approached for data if they met the inclusion criteria. If agreed, information was taken from them through structured questionnaire and their diabetic book or papers. Their blood pressure was recorded and also height and weight were recorded. The interview was conducted during their wait to see the doctor. In some cases, their turn came before the interview was over. Then they were asked to return after the check-up, which nobody refused.

viii. Data collection period:

Data were collected from 7th December 2014 to 23rd February 2015. No assistants were recruited.

ix. DIAGNOSTIC CRITERIA FOR GDM:

The Diagnostic Criteria Recommended by WHO in 2013 is followed by the hospital [35].

Gestational diabetes mellitus should be diagnosed at any time in pregnancy if one or more of the following criteria are met:

- Fasting plasma glucose 5.1-6.9 mmol/l (92 -125 mg/dl)

- 2-hour plasma glucose 8.5-11.0 mmol/l (153 -199 mg/dl) following a 75g oral glucose load.

x. Variables:

The main dependent variable in this study is use of hormonal contraceptives. Type of the contraceptive and duration of use was noted.

Other variables of interest were also noted through structured questionnaire:

1. Socio-demographic Risk Indicators: Maternal Age, Level of education, Occupation, Household expenditure.

2. Obstetric Risk Indicators: Parity, loss of pregnancy, Complication and Adverse outcomes of pregnancy, mode of delivery of previous pregnancy.

3. Familial Risk Indicators: History of GDM and Diabetes in family.

4. Medical condition and medication as Risk Indicator: History of chronic diseases and medication, polycystic ovary and menarche.

5. Life Style Risk Indicators: History of physical activity, smoking and other tobacco use.

DEFINITION OF THE VARIABLES:

Demographics:

Age: Current age of the patient with GDM

Education: Number of years of attending educational institute. The years of attendance were grouped into Illiterate, Primary, Secondary, Bachelors and Masters using the Bangladeshi educational system.

Occupation: Occupational Status was divided into Housewife, Employed, Unemployed and students. All job seekers were considered unemployed.

Family members: Number of persons living under the same roof who prepare and eat meals together.

Monthly Household Expenditure: Monthly expenses of a family in Bangladeshi Currency.

Contraceptive History:

Use of Hormonal Contraceptives: If the participant used any kind of contraceptives or not.

Type of Contraceptive: Type of hormonal contraceptive used by the participant.

Duration: Duration of use of hormonal contraceptives in years.

Use of OCP for other reason: has there been usage of Oral Contraceptive Pills for Gynecological reason. If yes, at what age and duration of use.

Obstetric History:

Gestational week: The gestational week when the Diabetes was diagnosed first.

Number of Conception: How many times the participant has conceived including the current pregnancy.

Number of Living Children: The number of living children the participant has.

GDM in previous pregnancy: Has the patient suffered from GDM in any previous pregnancies or not?

Loss of pregnancy: If the participant has lost any pregnancy, was it through abortion (loss of pregnancy before 24 weeks) or Still Birth (loss of pregnancy after 24 weeks)

Adverse Outcome: If the participant has suffered any adverse outcome in previous pregnancies, such as pre-term or post-term delivery, eclampsia, puerperal sepsis or any other complication.

Adverse outcome of the child: If the child of the participant suffered any adverse outcome such as congenital anomaly, low birth weight, macrosomia, neonatal jaundice, Respiratory distress syndrome or any other complication.

Mode of Delivery: Mode of delivery of the last child, if Normal Vaginal delivery or Caesarian section or assisted vaginal delivery with ventouse or forceps.

Plan of Birth Spacing: If the birth spacing plan is more than two years or less than two years.

Contraceptive failure: Whether this pregnancy is due to contraceptive failure or not.

Family History:

GDM: If any first degree relatives (parents, sibling or children) in the family had GDM.

DM: If any first degree relatives (parents, sibling or children) in the family have DM

Other Medical Condition:

If the patient is suffering from any other chronic condition such as Hypertension, Asthma, Thyroid Dysfunction , Poly-cystic Ovary or any other diseases.

If yes, whether the patient is being treated with any medication and how long has been the treatment going on.

Lifestyle:

Exercise: Participants were asked if they are engaged into any sort of physical exercise. If yes, what was the type of exercise, how often they did it and the duration of each session.

Habitual Addictions: Participants were asked about smoking, tobacco, zarda or betel leaf addiction.

Height: Height recorded on the visit.

Weight: Weight recorded on the visit.

BMI: Body mass index was calculated by weight (in kg) divided by height (in meter) squared.

Blood Pressure: Systolic and Diastolic blood pressures were recorded.

Lab Investigations: Hemoglobin levels, Blood sugar level of Fasting or after breakfast or Glucose, whichever was most recent were recorded. Any other available report was recorded too.

xi. Measurements

Blood Pressure Recording:

Blood Pressure (BP) was recorded after administration of the questionnaire. The pressure was measured in sitting position on the right arm by adult cuffs fitted with a standard mercury sphygmomanometer, placing the stethoscope bell lightly over the brachial artery. Two readings were taken 5 minutes apart, and the mean of the two was taken for recording of the individual. Hypertension was defined as systolic blood pressure (SBP) of 140 mm Hg or diastolic blood pressure (DBP) of 90 mm Hg [37].

Anthropometric Measurement:

Anthropometric measurements included height and weight. The measurements were taken without shoes and with light clothes. Height and weight were measured by using the machine present in the interviewing room; the machine is a weight machine in kilograms (kg) with an

attachment of stadiometer in centimeter (cm). Weight was measured while wearing light clothes by an adjusted scale and recorded to the nearest 0.1 kg. Height was measured with the stadiometer by standing upright. Both measurements were taken without shoes. Measurements were taken twice and the mean of them were recorded for each individual. BMI was calculated by the formula of weight in kilograms divided by height in meter squared. Unfortunately pre pregnancy measurements or BMI were not available to estimate the pregnancy weight gain.

xii. Data handling and analysis:

Each case was given an identification number to avoid confusion and mixing up. Data for every participant were checked by cross matching with the questionnaire.

Data were then entered into IBM Statistics SPSS 22 and analyzed using both IBM Statistics SPSS 22 and StataSE 13. All descriptive statistics for both categorical and continuous data were done in IBM Statistics SPSS 22. The T-independent test was used in IBM Statistics SPSS 22 to compare the means of different clinical parameters between users and non-users. Differences in FBG and ABF means for different age groups were analyzed using ANOVA. Proportions were estimated to establish relationships between categorical variables using cross tabulations. Comparisons of the proportions and graphing were done in StataSE 13.

xiii. Ethical issues:

Approval from Ethical Review Committee in Norway was taken to conduct the study. In Bangladesh, Ethical Clearance was approved by BIRDEM.

Prior interviewing, each participant was informed about the purpose and objectives of the study. They were assured about the confidentiality of their information. It was made clear that it is possible to withdraw at any point. Participation was voluntary and without any connection to treatment. Any curiosity and questions were welcomed and answered properly. Verbal consent of the participant was taken in presence of a witness. Information was handled with highest possible degree of confidentiality. Psychological conditions of the participants were considered sincerely and counselling was done if needed.

STUDY RESULTS and FINDINGS

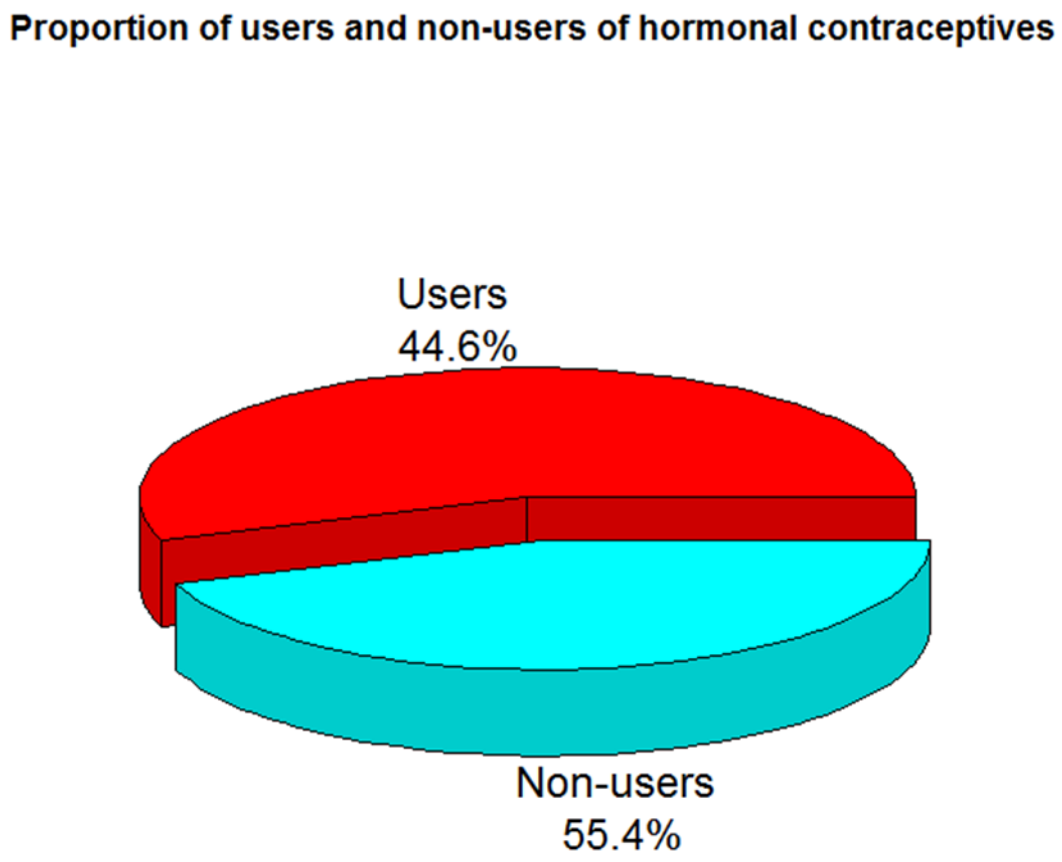

Figure 6: Pie chart of the proportion of users and non-users of hormonal contraceptives

Out of the 249 participants with Gestational Diabetes Mellitus, Hormonal Contraceptive Users were 111 (44.6%) and non-user of Hormonal Contraceptive was 138 (55.4 %).

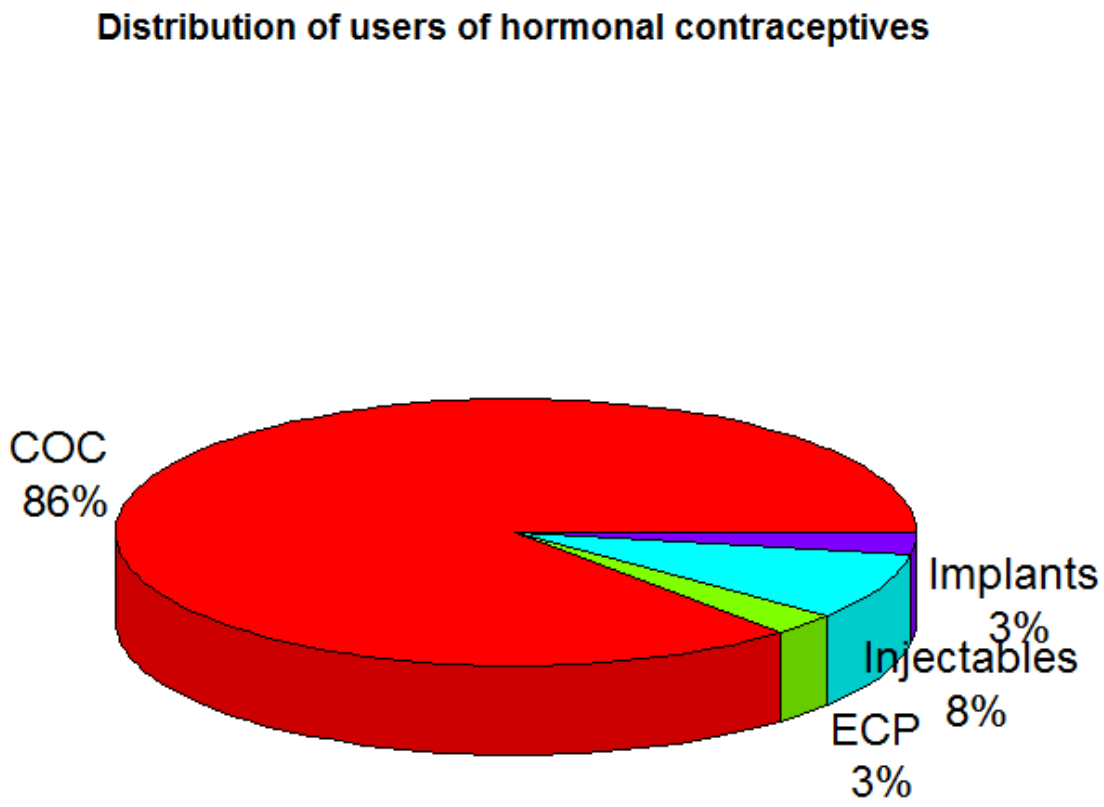

Figure 7: Pie chart of the types of contraceptives used by the participants

Among the Hormonal Contraceptive Users, the majority (86%) used Combined Oral Contraceptive in low dose. 8% used Injectable and 3% uses Implants and Emergency Contraceptive Pills each.

Table 1: Proportion of users and non-users of different types of contraceptives by demographic factors.

Demographic Factors	Non-Users n (%)	Users					Overall n (%)	P-value
		COC n (%)	ECP n (%)	Injectables n (%)	Implants n (%)	Total of users n (%)		
N	138 (55.4)	96 (38.6)	3 (1.2)	9 (3.6)	3 (1.2)	111 (44.6)	249 (100)	0.46
Age groups:								
≤ 25 years	21 (8.4)	19 (7.6)	0 (0.0)	2 (0.8)	0 (0.0)	21 (8.4)	42 (16.9)	1.00
26 – 29 years	41 (16.5)	34 (13.7)	3 (1.2)	4 (1.6)	0 (0.0)	41 (16.5)	82 (32.9)	1.00
≥ 30 years	76 (30.5)	43 (17.3)	0 (0.0)	3 (1.2)	3 (1.2)	49 (19.7)	125 (50.2)	0.18
Education:								
Illiterate	4 (1.6)	4 (1.6)	0 (0.0)	1 (0.4)	0 (0.0)	5 (2.0)	9 (3.6)	0.74
Primary	12 (4.8)	10 (4.0)	0 (0.0)	2 (0.8)	0 (0.0)	12 (4.8)	24 (9.6)	0.73
Secondary	42 (16.9)	44 (17.7)	0 (0.0)	6 (2.4)	0 (0.0)	50 (20.1)	92 (36.9)	0.20
Higher Secondary	19 (7.6)	15 (6.0)	0 (0.0)	0 (0.0)	2 (0.8)	17 (6.8)	36 (14.5)	0.87
Graduate	43 (17.3)	11 (4.4)	1 (0.4)	0 (0.0)	1 (0.4)	13 (5.2)	56(22.5)	0.01
Post-graduate	18 (7.2)	12 (4.8)	2 (0.8)	0 (0.0)	0 (0.0)	14 (5.6)	32 (12.9)	1.00
Occupation:								
Housewife	96 (38.6)	79 (31.7)	3 (1.2)	8 (3.2)	3 (1.2)	93 (37.3)	189 (75.9)	0.85
Employed	30 (12.0)	14 (5.6)	0 (0.0)	1 (0.4)	0 (0.0)	15 (6.0)	45 (18.1)	0.52
Unemployed	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	-
Student	9 (3.6)	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	12 (4.8)	0.83
Gravida								
Primi	69 (27.7)	18 (7.2)	3 (1.2)	3 (1.2)	0 (0.0)	24 (9.6)	93 (37.3)	0.07
Multi	69 (27.7)	78 (31.3)	0 (0.0)	6 (2.4)	3 (1.2)	87 (34.9)	156 (62.7)	0.34
Age in years [Mean ± SD]	30.4 ± 4.1	29.0 ± 3.7	28.7 ± 0.6	28.6 ± 3.4	34.7 ± 1.5	29.1 ± 3.7	29.8 ± 4.1	0.14‡

Table 1 shows the demographic characteristics of the participants. There were 111 contraceptive users, representing 44.6% of the sample and 138 non-users, representing 55.4% of the study group as shown in Figure 1. The average age of women who used hormonal contraceptives was 29 years compared to 30 years for non-users. This difference in mean age was not statistically significant (P = 0.14). For all demographic factors, the majority of the users of hormonal contraceptives were using COC. For example, COC was used by 7.6% of the women who were ≤ 25 years compared to ECP (0%), injectable (0.8%) and implants (0%) in the same age group. The proportion of users and non-users in the age groups ≤ 25 years and 26 – 29 years were identical. Although there were more users than non-users in the age group ≥ 30 years, the analysis showed that this could have been by chance (P = 0.18). On a P = 0.01, most graduates were non-users (17.3%) compared to users (5.2%). This could be due to graduates being aware of the side effects associated with hormonal contraceptives; hence they could be using other contraceptives. The proportion of users among housewives, employed women, unemployed women and students was higher compared to non-users, but the results were also not significant. Most primi gravida women were users (27.7%) compared to the non-users (9.6%) and most multi gravida women were non-users (34.9%) whereas the proportion of users was (27.7%). The analysis also showed that there was no evidence to suggest that gravida was different between users and non-users.

Table 2: Comparison of mean values of clinical parameters between non-users and users of hormonal contraceptives

Clinical parameters	Non-users	Users	95% CI for the mean difference	P-value
	Mean (95 % CI)	Mean (95 % CI)		
Systolic BP	113.80 (111.76, 115.85)	114.05 (111.93, 116.18)	-0.25 (-3.21, 2.71)	0.87
Diastolic BP	76.30 (75.14, 77.47)	74.73 (73.47, 75.99)	1.6 (-1.13, 3.29)	0.07
Hemoglobin	12.33 (12.17, 12.49)	12.06 (11.88, 12.24)	0.28 (0.04, 0.52)	0.03
FBS	5.65 (5.47, 5.83)	6.03 (5.59, 6.47)	-0.38 (-0.85, 0.10)	0.12
ABF	7.86 (7.53, 8.18)	8.88 (8.14, 9.61)	-1.02, (-1.82, -0.22)	0.01
BMI	28.75 (28.17, 29.34)	28.62 (27.96, 29.28)	0.13 (-0.74, 1.01)	0.77

The mean values of clinical parameters between non-users and users of hormonal contraceptives were compared as shown in Table 2. Significant differences in hemoglobin (P = 0.03) and ABF (P = 0.01) were observed. Hormonal contraceptive users had significantly lower hemoglobin levels but significantly higher ABF. Although the analysis also showed that users of hormonal contraceptives had higher mean values of SBP and FBS but lower values of DBP and BMI, these findings were shown not be statistically significant.

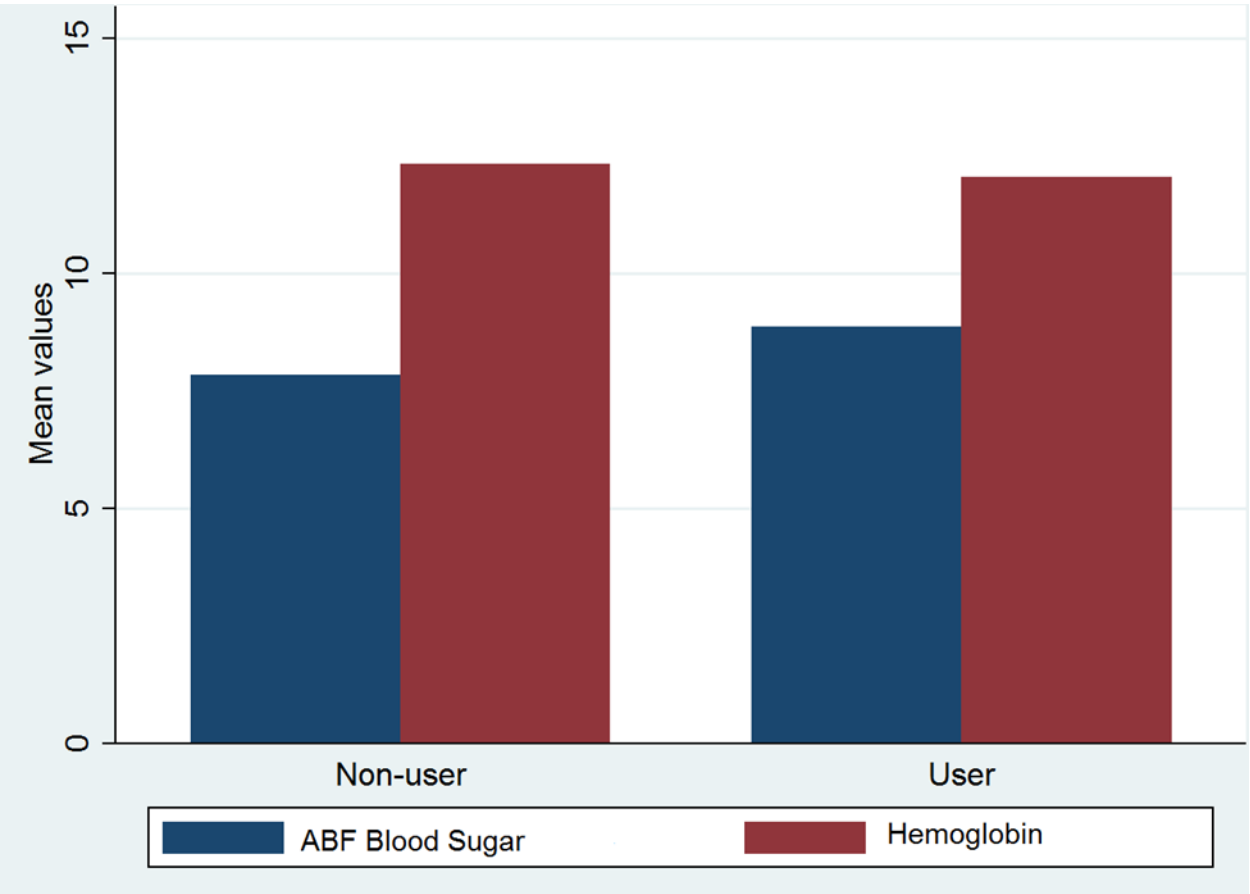

Figure 8: Bar graph of the difference in mean values of ABF Blood Sugar and Hemoglobin among the users and non-users of Hormonal Contraceptive

This Bar Graph portrays the difference in mean values of ABF Blood Sugar and Hemoglobin among the users and non-users of Hormonal Contraceptive.

Table 3: Mean values of FBG and ABF and their 95% CI for different age groups and family history of DM

Age groups			
	≤ 25 years	26 – 29 years	≥ 30 years
FBG [mean (95 % CI)]	5.59 (5.10, 6.07)	6.07 (5.66, 6.48)	5.74 (5.43, 6.05)
ABF [mean (95 % CI)]	8.33 (7.34, 9.32)	8.73 (7.95, 9.51)	8.04 (7.59, 8.49)
Family history of DM			
	Yes	No	Not known
FBG [mean (95% CI)]	5.96 (5.68, 6.23)	5.51 (5.16, 5.86)	4.90 (4.47, 5.33)
ABF [mean (95 % CI)]	8.58 (8.10, 9.06)	7.72 (7.17, 8.26)	6.37 (4.93, 7.80)

Differences in mean values of FBG and ABF for women in different age groups and whether they have a history of DM in their families are presented in Table 3. Women in the age group 26 – 29 had higher mean values of both FBG and ABF than women in the age groups ≤ 25 years and ≥ 30 years. Higher mean values of FBG and ABF were also observed among women with a family history of DM.

Table 4: Comparison of proportion of users and non-users of contraceptives with GDM by demographic factors

Demographic Factors	Users n (%)	Non-users n (%)	Difference in proportion	P-value for Test of proportion
Age groups:				
≤ 25 years	21 (8.4)	21 (8.4)	0 (0)	1.00
26 – 29 years	41 (16.5)	41 (16.5)	0 (0)	1.00
≥ 30 years	76 (30.5)	49 (19.7)	27 (10.8)	0.18
Education:				
Illiterate	5 (2.0)	4 (1.6)	1 (0.4)	0.48
Primary	12 (4.8)	12 (4.8)	0 (0)	1.00
Secondary	50 (20.1)	42 (16.9)	8 (3.2)	0.35
Higher Secondary	17 (6.8)	19 (7.6)	-2 (0.8)	0.46
Graduate	13 (5.2)	43 (17.3)	-30 (12.1)	0.01
Post graduate	14 (5.6)	18 (7.2)	-4 (1.6)	0.22
Occupation:				
Housewife	96 (38.6)	93 (37.3)	3 (1.3)	0.85
Employed	30 (12.0)	15 (6.0)	15 (6.0)	0.52
Unemployed	3 (1.2)	0 (0.0)	3 (1.2)	-
Student	9 (3.6)	3 (1.2)	6 (2.4)	0.83
Gravida				
Primi	69 (27.7)	24 (9.6)	45 (18.1)	0.07
Multi	69 (27.7)	87 (34.9)	-18 (-7.2)	0.34

Table 4 is a comparison in proportion of users (combined) and non-users of hormonal contraceptives with GDM by demographic characteristics. The proportion of users and non-users in the age groups ≤ 25 years and 26 – 29 years were identical. There were significantly more users than non-users in the age group ≥ 30 years. Most post graduates women were non-users (7.2%) compared to users (5.6%). However, the analysis also showed that this could be by chance (P = 0.22). The proportion of users among housewives, employed, unemployed and students were all higher than non-users, but the results were also not significant. Most primi gravida women were users (27.7%) compared to non-users (9.6%) and most multi gravida women were non-users (34.9%) whereas users were 27.7%. The analysis showed no significant differences here as well.

Table 5: Table 5 Comparison of proportions between users and non-users of hormonal contraceptives by known risk factors of GDM

Risk Factors of GDM	N	User n (%)	Non-User n (%)	P-value
Age:				
≤25	42	21 (50.0)	21 (50.0)	0.5
26-29	82	41 (50.0)	41 (50.0)	0.5
≥30	125	49 (39.2)	76 (60.8)	0.01
Gravidity:				
First	93	24 (25.8)	69 (74.2)	< 0.01
Second	84	51 (60.7)	33 (39.3)	0.03
≥ 3	72	36 (50.0)	36 (50.0)	0.5
GDM in previous pregnancy:				
Yes:	9	6 (66.7)	3 (33.3)	0.17
No:	123	75 (61.0)	48 (39.0)	0.01
Not known	21	6 (28.6)	15 (71.4)	0.04
Family History of GDM:				
Yes	18	3 (16.7)	15 (83.3)	0.01
No	225	108 (48.0)	117 (52.0)	0.27
Not Known	6	0 (0.0)	6 (100.0)	-
Family History of DM:				
Yes	177	57 (32.2)	120 (67.8)	< 0.01
No	69	51 (73.9)	18 (26.1)	< 0.01
Not known	3	3 (100.0)	0 (0.0)	-

The analysis presented in Table 5 is a comparison of the proportion of women who used hormonal contraceptives and those who did not by known risk factors of GDM. The proportion of non-users of hormonal contraceptives who were at least 30 years (60.8%) was significantly higher than those who used hormonal contraceptives (39.2%). The majority of first gravida were non-users (74.2%) of hormonal contraceptives compared to 25.8% users ($P < 0.01$). However, the proportion of users of hormonal contraceptives was higher among second gravida women (60.7%) compared to non-users (39.3%). It was also observed that women with at least gravida 3 were equally likely to be users as there are non-users. Women who did not have GDM in their previous pregnancy were more likely to be users (61%) than being non-users (39%). The proportion of women who did not know their GDM status in their previous pregnancy was significantly higher among non-users (71.4%) compared to users (28.6%). For those with a family history of GDM, the majority were non-users of hormonal contraceptives (83.3%) compared to users (16.7%). This was also true for women with a family history of DM. 67.8% of the women from families with a history of DM were non-users of hormonal contraceptives compared to 32.2% who were users.

Table 6: Logistic regression models showing risk factors for severe hyperglycemia (≥ 8 mmol/L)

	Model 1		Model 2		Model 3		Model 4	
	OR (95 % CI)	P-value	OR (95 % CI)	P-value	OR (95 % CI)	P-value	OR (95 % CI)	P-value
Referent: users								
Non-users	0,78 (0,47, 1.31)	0,35	0,75 (0,44, 1.25)	0,27	0,75 (0,45, 1.27)	0,29	1.00 (0,57, 1.76)	0,99
Referent: >30 years								
≤ 30 years			0.65 (0.39, 1.10)	0.11	0,68 (0,40, 1.15)	0,15	0.65 (0.38, 1.12)	0.12
Referent: BMI > 25								
BMI ≤ 25					0.68 (0.33, 1.40)	0.30	0.61 (0.29, 1.27)	0.19
Referent: No DM Family history								
Family history of DM							2.14 (1.11, 4.15)	0.02

Risk factors for severe hyperglycemia are presented in Table 6 in the form of odds ratios (OR) and their 95% CI using the step-wise binary logistic regression model. Model 1 is the unadjusted effect of using hormonal contraceptives on severity of hyperglycemia whereas models 2, 3 and 4 show the effect of using hormonal contraceptives after controlling for age, BMI and family history of DM. All four models show that using hormonal contraceptives has no bearing on the severity of hyperglycemia. This means that there is no evidence to suggest that hormonal use increases the risk of severe hyperglycemia, even after controlling for age, BMI and family history of DM. The analysis also revealed that age and BMI were not significant predictors of hyperglycemia. However, the risk of severe hyperglycemia was significantly higher by 2.14 among women with family history of DM compared to women who did not have any family history of DM (P = 0.02).

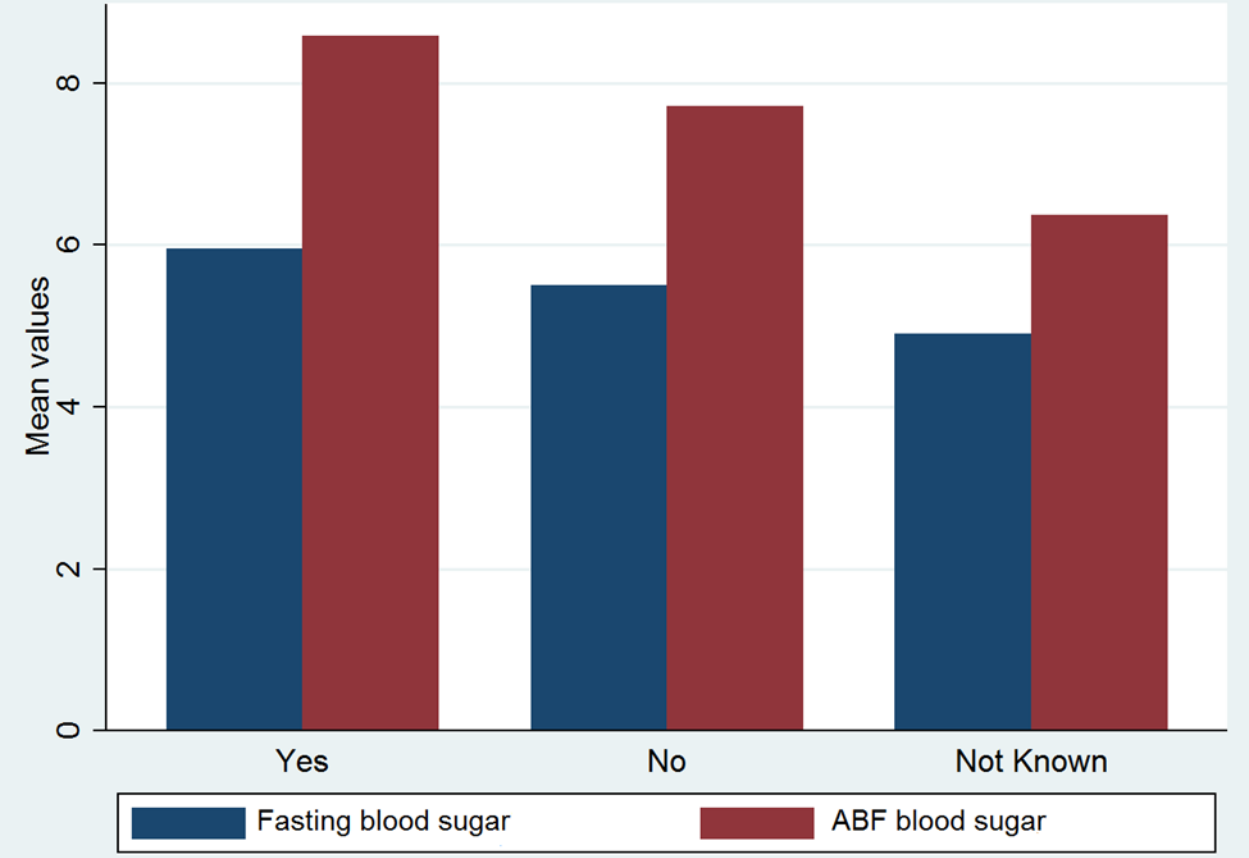

Figure 9: Bar graph of differences in severity of hyperglycemia among the participants with positive family history of DM

Bar Graph showing the differences in severity of hyperglycemia among the participants with positive family history of DM.

Contraceptive Failure:

Among the 249 pregnancies, 18 were due to contraceptive failure. Among those 18 pregnancies, 12 were hormonal contraceptive users and 6 were non-hormonal contraceptive users. The improper usage of hormonal contraceptives can be a contributing factor to this.

Mode of Delivery:

120 of the 249 participants have given birth before. Modes of delivery were Normal Vaginal Delivery for 72 and Lower Uterine Caesarian Section for 48 cases or 40% of the Caesarian section among the deliveries; a number that is quiet high.

Loss of Pregnancy:

75 cases among 249 have suffered from loss of pregnancy in their previous pregnancies. 39 of them were lost in abortion and 36 in still birth. Among these 75 cases, only 6 patients were diagnosed with GDM them, 48 of them claimed to be with normal glycemic status and 21 admitted to be ignorant of their glycemic status.

DISCUSSION

This study was done with an objective of examining the relation between Gestational Diabetes Mellitus and Hormonal Contraceptive. Specific interest was to see if GDM is more common in hormonal contraceptives users of Bangladesh. It was also an objective to check the association of glycemic severity with hormonal contraceptive in women with GDM. Although not much research has been conducted in this arena of interest, reviewed studies suggested the possibility of association between hormonal contraceptive and gestational diabetes mellitus [3, 4, 29, 30].

The study was designed as an observational study based on the outpatient department of a hospital with specialty in diabetic care. The ideal study design would have been a case control study to estimate the risk association. Furthermore, a community based prospective study would have been more appropriate for a study like this. However, for the control group, other general hospital had to be used for data collection and would have required more time and logistics. Similarly, a prospective study would have asked for much more time and resources. Due to limitation of time and logistics and proper health infrastructure in Bangladesh, the most convenient option was to do a hospital based study which is observational. Data was collected retrospectively from women with GDM who came for antenatal checkup.

BIRDEM-2 was selected as the hospital of choice as it provides comprehensive care for pregnant women with diabetes. The hospital service coverage is from antenatal checkup, delivery to paediatric care for the newborn of the diabetic mothers. Even from other fully equipped tertiary care hospitals of the city, many cases of diabetic pregnancies are referred to BIRDEM for optimum diabetic care. This hospital is also economically inexpensive. It has a free of cost social welfare service towards extremely poor patients. Also, this hospital is affordable by lower middle class and lower class. Thus, to get the bulk of patients with GDM in order to complete the sample size, no other hospital could have been a better choice.

The interview had to be conducted in room 217 of BIRDEM-2. This room is the office of 3 doctors. One doctor attends patient with pregnancies to control their blood sugar. Other two doctors attend non-pregnant patient with other medical problems. All patients in this room are women. There are one medical assistant and one clerk to help calling in the patients and help

taking the anthropometric measurements. There are also seat for three patients to wait for their turn when three patients are being attended by three doctors. Interview was conducted while patients waited inside the room. Separate room or even a separate corner was not possible to obtain as the authority speculated that would create confusion among the patients. However the arrangement was, the interviews went uneventfully. The doctors and the staff were extremely helpful and the participants were very co-operating. The blood pressure and anthropometric measurements of the patients are usually taken by the medical assistant present at the room; but the participants' were taken by the researcher herself.

Indeed the room was overcrowded and privacy was not well maintained, however none of the participants objected to this arrangement. Only many of them hesitated and refused to disclose their monthly household expenditure which is considered private and not to be disclosed outside the family. Because of the hospital environment it was easier to talk about more personal issues like contraceptives and diseases. Apart from money and expenditure being a personal matter, some of the women were not aware of it too. Though changing nowadays, many Bangladeshi families are still patriarchal and women are not always included in economical decision.

The decision of choosing the method of contraception also depends largely on husbands. In some cases, husbands are the one to introduce hormonal pills by getting them from pharmacies. In other cases, it was noticed that women mostly choose their contraceptive method by peer suggestions. None of the participants visited health care professional to seek advice before choosing contraception method. Along with the peer suggestion, attractive advertisement on TV, print media and billboards influenced their decision. The few who used injections and implants came from rural areas where they were visited by field workers for health promotion. In rural areas of Bangladesh, clinical trial of injections and implants has been going on for decades. There had been controversies regarding unethical approach and violation of human rights about some of the trials. Implant Norplant and Injectable Depo-Provera are the most criticized ones because of their side effects and also for not providing complete information about the drugs being in a trial [38, 39, 40]. Unfortunately the users of injectable

and implant hormonal contraceptives could not name the brand they have been using. If the study was done in a rural area, there could be the chance to have more participants as injectable and implant users which might had lead the result in a different way. Injectable and Implants are more commonly used in rural areas, in cities oral pills are the most popular choice.

The diagnostic criteria for GDM used in this study are the standard criteria set by World Health Organization in 2013. According to the criteria, gestational diabetes mellitus can be diagnosed at any time in pregnancy if fasting plasma glucose is within 5.1-6.9 mmol per liter and/or following a 75g oral glucose 2 hour plasma glucose is 8.5-11.0 mmol per liter.

To get the GDM patients precisely, only participants whose diabetes is diagnosed within 24 to 28 weeks of pregnancy are chosen. Because of the lack of proper health care facility and awareness, many women visit a doctor for the first time in their life when they are pregnant. For this reason, some of the patients who could be suffering from DM before conception only get diagnosed during pregnancy and are labeled as GDM. To avoid these cases as much as possible, participants with GDM diagnosed later in pregnancy are taken. Continuous Sampling Technique was used to reach the required number of sample size; which has been achieved.

Sample size was calculated as 246 by presuming that 20% women with GDM will be non-hormonal contraceptive user. On field, 249 women with Gestational Diabetes Mellitus aged from 22 years to 39 years participated in the study after giving informed consent. 111 of them were hormonal contraceptive users and 138 were non-users of hormonal contraceptives. It must be noted that, by the mention of 'non-user group' in the study, it is only meant that the group does not use hormonal contraceptive; not necessarily they are non-users of other methods of contraception.

The principal data source is the information provided by the participants. There is no existing health registration or systemic patient profile in Bangladesh. Recall problem and misleading information from the participant could not be verified for that reason. As there is not much of practice to preserve patient history, the information available in the patient's book/prescriptions are often incomplete and insufficient or even lost by the patient.

The analysis of the result shows that among the GDM mothers, 44.6 % are hormonal contraceptive users and 55.4% are non-users. Here, the user group (86%) comprises mainly combined of oral contraceptive in low dose. There were only a few who were using implants and injections. Had there been more injectable and implant users, there could be a difference in proportion, as previous study by Hedderson et al. suggested that high androgenic hormonal contraceptive increase the risk of GDM [29].

Differences between the users and non-users of hormonal contraceptives on the basis of demographic factors such as age, education, occupation, parity were checked. There were no significant differences that were found. However, the study revealed that higher proportion participants with higher education in the non-user group. Also, the average age of non-user group (30 years) is one year more than the user group (29 years). Although there is no statistical significance, this could be due to awareness of the side-effect of the hormonal contraceptive in more matured and educated women.

Among 249 women, 93 were with first pregnancy and 156 had been pregnant before this ongoing pregnancy. Among them, 9 women confirmed to be suffering from GDM in their previous pregnancy. 6 of them continued use of hormonal contraceptives till this current pregnancy.

Comparison of the mean value of clinical parameters between user and non-user group showed significant differences in hemoglobin levels and after breakfast glycemic levels. The user group had lower hemoglobin level (12.06 opposed to 12.33 in non-users) but higher After Breakfast Blood (ABF) sugar level (8.88 opposed to 7.86 in non-users). A previous study by Petitti D.B on the effects on combined oral contraceptives [36] implied that hemoglobin level is rather increased in women who use oral hormonal contraceptives, which is 86% of the user group in this study. As the oral hormonal contraceptive diminishes and regulates the menstrual bleeding, the user is less prone to be anemic. [36].The significantly lower level hemoglobin with extremely small mean difference of 0.28 in user group in this study could possibly be co-incidental. Although the mean difference is very small (1.02), the higher level of After Breakfast Blood Sugar level (ABF) among the user group is significant. It might be due to the lingering

effect of progestin from the usage of hormonal contraceptive which is affecting the glycemic control.

Another observation is that mean values of both Fasting and After Breakfast Blood Glucose levels are slightly higher in age group 26-29 years (FBG- 6.07, ABF-8.73). Whereas, in less than or equal to 25 years is FBG- 5.59, ABF- 8.33; and in 30 or more years it is FBG- 5.74, ABF- 8.04. However, it remains unclear what factor caused this difference. There remains the possibility of co-incidence because of small sample size.

The similar result is also observed in participants with positive family history of DM. The mean values are, FBG- 5.96, ABF- 8.58 for participants with family history of DM. For participants without family history the results are, FBG- 5.51, ABF- 7.72 and for unknown family history, FBG- 4.90, ABG-6.37. Whereas, participants coming from a family with diabetic people are expected to be more used to and in control of glycemic status, it has not been the case. It could be due to the fact that, repeated exposure and familiarity of the disease has diminished its sense of severity. Whatsoever, these results are irrespective of hormonal contraceptive usage.

Most primi gravida women are accounted as users whereas multi gravida are non-users. This could probably be due to the advice and counseling by health personnel. It is seen that women who had GDM in previous pregnancy are less likely to use Hormonal Contraceptive. Again, it can possibly due to be the advice of the physician.

Severity of hyperglycemia (≥ 8 mmol/L) has been calculated against the usage of hormonal contraceptive. There is no result that proves use of hormonal contraceptive can be linked with severe hyperglycemia. Even after adjusting with age, BMI and family history of DM, no evidence suggest that hormonal contraceptive increases risk of poor glycemic control. Yet, the analysis shows that the risk of hyperglycemia is 2.14 time higher among participants from positive family history of DM (OR 2.14, P= 0.02).

8mmol/L has been chosen as the cut-off point for severity of hyperglycemia because this is the standard cut-off point for random blood glucose test in an individual. In pregnancy it is expected to keep the Fasting blood glucose ≤5.2 mmol/L and post prandial ≤6.6 mmol/L

according to American Diabetic Association [41]. However, in the study hospital it is practiced to maintain the blood sugar level ≤5.0 mmol/L in fasting state and ≤7.0 mmol/L in post prandial state. Compared to the decreased range of blood sugar in pregnancy, 8mmol/L can be considered severe hyperglycemia.

It should also be noted that among the participants, 71.1% of the GDM patients have family history of Diabetes Mellitus.

Unfortunately, 7.22% of the pregnancies in this study are a result of contraceptive failure. 66.67% of the contraceptive failed pregnancies are among the hormonal contraceptive users. Although the use of hormonal contraceptive (Oral pills in particular) is widely used in mass, it can be implied that proper use is yet to be achieved.

The number of caesarian section in previous pregnancies of multi gravid women is alarmingly highly (40%). Though the average percentage of Caesarian section in Bangladesh is 17.1%, the higher percentage here could be due to the fact that this study is done in an urban hospital and patients are in proximity to surgical facility. It was not possible to evaluate the justification of the caesarian sections because of the lack of medical history and documents.

It was a positive finding to see that each and every participant had the knowledge of birth spacing to be two years.

Strength and Limitation of the study

Acknowledging that 46.4% women with pregnancy never visit hospital for ante-natal checkup, this study is not without deficit. Yet, this study has its own strengths and limitations.

Strength of the study:

One considerable strong point of this study is the use of proper diagnostic criteria. The diagnostic criteria used are suggested by world health organization. Also the laboratory service is considered one of the best and most reliable in Bangladesh. Careful scrutiny of the results was performed to choose the GDM patients only.

The interviews for data collection in this study were conducted solely by the researcher. This is strength as it excludes differences of concepts and perception. Same maneuver of asking questions and equal marking was ensured on the questionnaire for all the participants.

Quality control was present in blood pressure measurement and taking anthropometric measurements as these were done by the researcher herself, who has experience as a trained medical professional.

Before the main study was initiated, a pretesting was conducted on a small scale of 5 patients. The questionnaire was adjusted accordingly and no major changed were needed.

All the above mentioned facts can be attributed as the strength of the study.

Limitations of the study:

A major limitation of this study lies in its design. Lack of a control group limits us from drawing any firm conclusion on the risk association of hormonal contraceptive and gestational diabetes mellitus. A much larger sample size in a population based study would have been most appropriate.

The data collection was solely dependent on the information provided by the participants. There was no possibility to cross check because of the lack of proper medical history. It is

possible that the participants might not were always accurate on providing the correct information. For this reason, there are chances of recall bias.

A tertiary hospital situated in the center of the capital was chosen for the study. Although patients from all over the country visit this hospital, it is majorly frequented by urban dwellers from surrounding area. This leads to the selection bias as large rural and peripheral population are left out. The ongoing political violence and blockade during the data collection period severely restricted patient visits from far areas.

Along with the selection bias because of the location, there is another biasness to be considered. This particular hospital is mostly visited by women from lower, lower-middle and middle class society. As this hospital is affordable and good service provider, the hospital remains very crowded and lacks the standard comfort in some areas. This drives the women of upper-middle and upper class society to seek treatment from a more private and posh facilities. It is to mention that, the consultants of those more expensive and better arranged facilities are mostly the same consultants of this hospital. Differences can be expected in lifestyle and demographic factors within different social classes.

A particular weakness of this study remains in the unavailability of previous medical records. It was not possible to cross check or understand the actual fact about previous pregnancies or outcome of the pregnancies. No record of pre-pregnancy BMI made it impossible to examine the pregnancy weight gain of the participants which is a considerable draw back. No confirmation of previous medical history makes it difficult to imply suggestions in many regards.

Confounding Effects:

It was not possible to calculate the pregnancy weight gain rate of the participants. Pre-pregnancy overweight/obesity or excess weight gain during pregnancy might have an association with GDM [42]. The risk of glycemic severity in participants who had pre-pregnancy overweight/obesity or gained excessive weight during pregnancy might have been confounded in the study.

Socio-economic status has the possibility to act as another confounding factor. With better socio-economic status, health care facility becomes more accessible and with better purchasing capability of food comes the risk of over-nutrition. The result where it is showed that patients with positive family history of DM has greater risk of hyperglycemic severity might be due to confounding effect of better socio-economic status. It could not be determined as many of the participants did not reveal monthly household expenditure. Increased Caesarian section can also be a result of better socio-economic status.

Validities of the study

Every study is conducted with an expectation for maximized validity both internal and external. However, ideal situation is not always possible to attain in a study. The internal and external validity of this study are discussed separately.

Internal Validity:

Internal validity of a study is estimated by the accuracy of its measurements of experimental techniques. That relates it to the instruments used. In this study the diagnosis of GDM was done based on worldwide accepted criteria. Also, the tests were run by the laboratory of BIRDEM which one of the best in the country before as mentioned before. Accuracy of blood pressure measurements and anthropometric measurements was present as they were taken by the researcher only. Data was also collected solely by the researcher. This is likely to increase the reliability of the data and results. These are factors increase the internal validity of the study.

A chance of recall bias which is mentioned in limitations hampers the internal validity of the study.

External Validity:

The sample population of this study represents urban or semi-urban women of lower to middle class background. The upper class scenario has a chance to be little different because of their privileged lifestyle including better accessibility to health care service. However, as the majority of the population of Bangladesh belongs to the lower to middle socio-economic background, it can be assumed that the finding of this study can be inferred on the pregnant women of Bangladesh. For this reason the study is more likely to be externally valid.

Implications:

Considering the fact that there has been no other studies conducted regarding hormonal contraceptives in Bangladesh, this study can provide a baseline data. According to the results, it might be considered that the oral hormonal contraceptives are safe to use without much risk of developing gestational diabetes mellitus. However, further research in a much larger scale is needed for confirmation.

Recommendation:

The analysis of data from this particular study generates several issues which need to be explored further.

The issue of hormonal contraceptives and gestational diabetes mellitus calls for a population based case control study to evaluate the situation in large scale.

Bangladesh is a country of limited resources in comparison to its population size. The increasing life expectancy with increase in non-communicable diseases is dramatically raising the expenditure of health care system. Continuation of this will soon become an overwhelming social burden. Awareness about non-communicable disease especially diabetes should become

the focus of the health care system. Beside the patient, the family members should be also warned about their increased risk and educated accordingly. Preventive measures need to be implicated. Measures should be taken to improve patient compliance to prevent complications. Without achieving patient compliance, complications can be avoid or deterred.

Importance of properly maintained medical records should be considered as a basic necessity. Regular check-up should be encouraged for the whole population, particularly among the women of reproductive age. Proper and thorough use of contraceptive methods needs to be encouraged to avoid unwanted pregnancies. Justification of the increasing prevalence of Caesarian section has to be evaluated as well.

Conclusion:

This study can be concluded with few key points.

According to the analysis, Combined Oral Contraceptives (low dose) seems to be safe to use as it appears not to play any role in glycemic control or developing Gestational Diabetes Mellitus.

Participants with family history of DM are suggestive to have poor control of blood sugar which might be the base of developing gestational diabetes mellitus.

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APPENDICES

Appendix-1: Questionnaire

QUESTIONNAIRE

Date:

Patient ID:

PART – A

- SOCIO-DEMOGRAPHIC DATA:

Sl.No	Variables	Response	Code
1.	Age	_____ years	
2.	Education	_____ years	
3.	Occupation	1. Housewife 2. Employed 3.Unemployed 4. Student	
4.	Number of family members- Monthly Household Income-	_____ persons BDT_____	
5.	Per capita Income	BDT_____	
6.	Monthly household expenditure	BDT_____	

- CONTRACEPTIVE HISTORY:

Sl.No	Hormonal Contraceptives	Response	Code
7.	COC		
8.	POP		
9.	ECP		
10.	Injectable		
11.	Implants		
12.	Duration of Use	____ years	
13.	Continuation	1. Yes 2. No	
14.	Use of OCP for gynecological reasons?(non-contraceptive use)	1. Yes 2. No	

15.	Duration-		
16.	At what age?		

- OBSTETRIC HISTORY:

Sl.No	Variables	Response	Code	Skip Pattern
20.	Gestational week?			
21.	Is this your First Pregnancy?	1. Yes 2. No		If yes, skip to 30.
22.	How many times have you conceived?	1. First 2. Second 3. Three or more		
23.	How many living children do you have?	1. None 2. One 3. Two 4. Three or more		
24.	Did you suffer from GDM?	1. Yes 2. No 3. Not Known		
25.	Have you lost any pregnancy	1. Yes 2. No		
26.	Lost in-	1. Abortion 2. Still Birth		
27.	Have you suffered any other adverse outcome?	1. None 2. Pre-term delivery 3. Post-term delivery 4. Eclampsia/Pre-eclampsia 5. Puerperial sepsis 6. Other_____		
28.	Did your child have any perinatal complication?	1. None 2. Congenital anomaly 3. Low Birth Weight 4. Macrosomia 5. Neonatal Jaundice 6. Respiratory Distress Syndrome 7. Other_____		
29.	What was the mode of delivery of your last child?	1. Normal Vaginal Delivery 2. Forcep/Suction delivery 3. Caesarian Section		

30.	Plan of Birth Spacing	1. Less than 2 yrs 2. Two or more		
31.	Is this pregnancy due to contraceptive failure?	1. Yes 2. No		

- FAMILY HISTORY:

Sl.No	Variables	Response	Code
32.	Do you have history of GDM in your family?	1. Yes 2. No 3. Not known	
33.	Do you have family history of Diabetes?	1. Yes 2. No 3. Not known	

- OTHER MEDICAL AND DRUG HISTORY:

Sl.No	Variables	Response	Code	Skip Pattern
34.	Are You Hypertensive?	1. Yes 2. No		If no, skip to 36.
35.	Duration-	_____ years		
36.	Do you have any other chronic condition?	1. Asthma 2. Thyroid Dysfunction 3. Other(Specify)		
37.	Are you on any kind of medication?	1. Steroids 2. Thyroid Supplement 3. Antihypertensive 4. Lipid Lowering 5. Other(Specify)		
38.	Duration-	_____ years		
39.	Polycystic Ovary	1. Yes 2. No		
40.	Age of Menarche	_____ years		

- LIFESTYLE:

Sl. No	Variables	Response	Code	Skip Pattern
41.	Do you exercise?	1. Yes 2. No		If no, skip to 44.
42.	How Often?	1. Daily (___ hours) 2. Once to Thrice a week 3. Other(specify)		
43.	Type of Exercise	1. Brisk Walking 2. Gym 3. Other (Specify)		
44.	Do you smoke?	1. Yes 2. No		If no, skip to 48.
45.	Duration-	_____ years		
46.	What do you smoke?	1. Cigarette 2. Biri 3. Others (specify)		
47.	Frequency	1. Daily (____sticks) 2. Occasionally		
48.	Do you take betel leaf?	1. Yes 2. No		
49.	Duration-	_____ years		
50.	Do you take Tobacco leaf/ Zorda?	1. Yes 2. No		
51.	Duration-	_____ years		

PART- B

Physical Examination:

Sl. No	Variables	Value
1.	Height	
2.	Weight	
3.	BMI	
7.	Systolic Blood Pressure	
8.	Diastolic Blood Pressure	

PART-C

Lab Investigations**:**

Sl.No	Investigations	Results
1.	FBG ABG	
2.	OGTT	
3.	Total Cholesterol (if available) Triglyceride HDL LDL	
4.	TSH (if available) FT4	

Appendix-2: Consent Letter

Invitation to participate

Dear Madam,

You have been asked to participate in a research project on Gestational Diabetes Mellitus and its risk association with Hormonal Contraceptive. The researcher will explain you in details about the study. Please feel free to ask questions.

Purpose of the study is to investigate whether hormonal contraceptive acts as a risk indicator for Gestational Diabetes Mellitus.

It is a project undertaken by the University Of Oslo, Norway.

A total of 246 pregnant women, diagnosed as cases of Gestational Diabetes Mellitus by screening on 24-28 weeks of pregnancy will be interviewed. History of Contraceptive use along with socio-demographic, obstetric, medical, family history will be recorded as necessary information for this study. Available medical records and Anthropometric measurement will be taken.

Participation in this study is voluntary and you have the full right to withdraw from the study whenever you want. Participation has no effect on your medical care. On the other hand you have the right to ask any question at any point.

Your information will be treated with highest possible degree of confidentiality. The result of the study will be in numerical data with no options to trace you back.

After knowing all the relevant information regarding participation in the research, if you have any question, please feel free to ask. If you do not want to participate, please feel free to refuse.

If you agree your verbal consent will be taken.

Do you agree to participate in the study? Yes No

Signature of the interviewer:

Date:

Participants ID No:

Appendix- 3: Photos

Figure 10: Patients waiting outside consultation room 217 (the room used for interviewing) in BIRDEM-2 hospital.

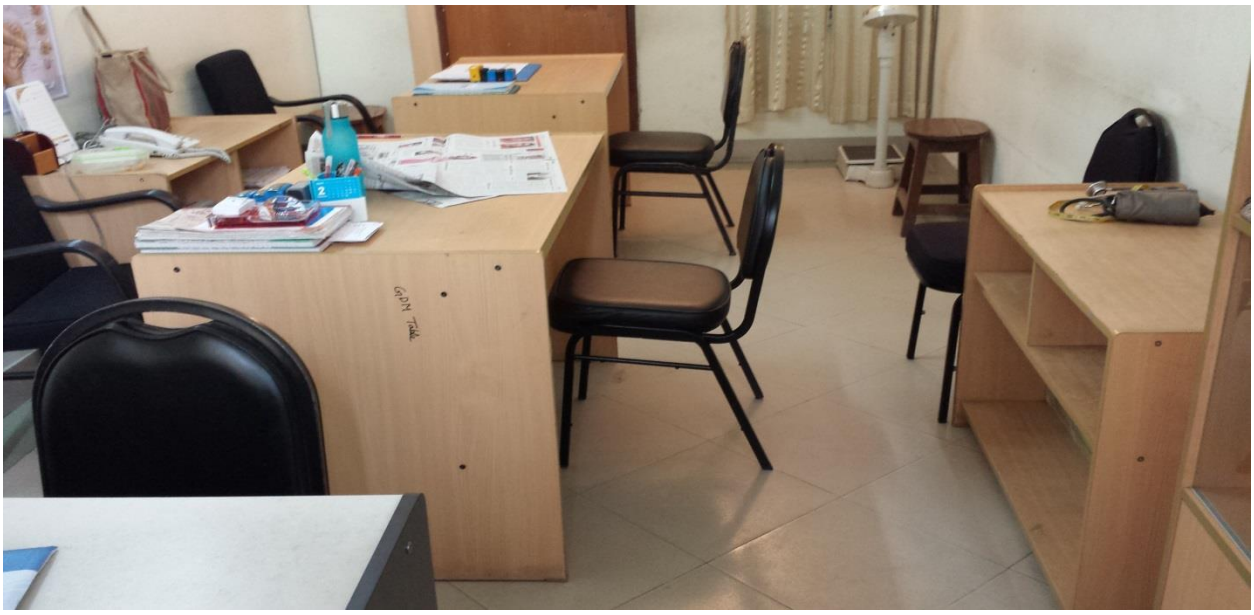

Figure 11: Inside the interviewing room. The middle table is used by the doctor who consults patients with GDM.

Figure 12: BIRDEM general hospital 2, Dhaka.