





dystocia [27]. PGDM occurrence is diagnosed before pregnancy. Pregnant women with pre-gestational type 1 and type 2 diabetes are more likely to have cesarean deliveries, macrosomic infants, fetal congenital malformations, and preterm deliveries [28].

The impact of hyperglycemia on adverse maternal and neonatal health outcomes is undoubtedly continuous. Although insulin therapy decreases the incidence of fetal macrosomia for those women with more severe grades of hyperglycemia, the extent of any effect on maternal and other neonatal health outcomes is uncertain [29]. Although both pre-gestational and gestational diabetes are strongly associated with higher birth weights, in the presence of vascular disease associated with diabetes, birth weight may be restricted [30].

### 3.1 Gestational Diabetes Associated Risk to the Mother

The immediate dangers to the mother with GDM are in the form of obstetric complications, such as pre-eclampsia, preterm deliveries, still births and caesarian sections [31], [32]. In Asian Indian women diagnosed with GDM reported to have 8.2% preterm deliveries [33]. There have also been reports of increased occurrence of cesarean section (30%), preeclampsia (20-30%), and polyhydramnios (20%) which can result in preterm labor [34]. Moreover, there are reports which show one in six GDM diagnosed Indian women who have persistent diabetes after the pregnancy was over [35]. During pregnancy, such women developed changes in their fasting lipid level, blood pressure, large and small vessel function which caused hypertensive complications such as pregnancy induced hypertension and pre-eclampsia. Further, during pregnancy there was development of insulin resistance causing a transient increase in lipid levels, representing a metabolic Syndrome like condition involving central obesity, plus any two of the following factors, raised triglyceride levels, reduced HDL cholesterol, raised blood pressure and raised fasting plasma glucose [36].

Periodic GDM pregnancies and the considerable risk (50 %) of developing Type 2 DM in 5-10 years is the long-term threat to the mother which are associated with GDM. In a Danish population study, 39.9% women with a mild form of GDM (treated by diet alone) had developed type 2 DM in 9.8 years after the index pregnancy [37, 38]. In another review, 2.6-70% women with GDM progressed to type 2 DM, when women were followed up from 6 weeks post-partum to 28 years post-partum and the lowest rates were found from studies that had the shortest follow-up period [39]. In another study involving a control group (without GDM), subjects were followed for a period of 11 years, the cumulative incidence for type 2 DM and abnormal glucose tolerance in women who had GDM was 13.8% and 42.2% respectively. It was 0 and 2.8% ( $P < 0.05$ ) respectively in women without GDM [40]. In an Indian retrospective study, crude prevalence of type 2 DM was 52% in women with GDM as compared to the 4% observed in women without GDM, conducted 4.5±2 years after the index pregnancy [35]. The development rate for type 2 DM in women with GDM indicated wide variation and discrepancies. The role of ethnicity in the increase of type 2 DM in women with GDM

remained controversial. In a UK study, 35% of the Indo-Asians had persistent glucose intolerance 3 months postpartum compared with 7% of Caucasians and 5% of the Afro-Caribbean subjects [39]. The effect of ethnicity became insignificant when the analyses were adjusted for duration of post-partum follow-up in a systematic review of several studies indicating that the data was not consistent on the role of ethnicity in development of type 2 DM in women with GDM [40].

Women with a history of GDM are at a greater risk of developing various chronic diseases later in life, other than diabetes, such as metabolic syndrome and cardiovascular disease compared to women who did not develop GDM. Data collected on parous women in a cross sectional analysis showed that women with prior GDM were more likely to have the metabolic syndrome compared to women who did not have GDM (86.6% vs. 73.5%;  $p = 0.001$ ). They also had a higher prevalence of CVD (15.5 vs. 12.4%, OR 1.85, 95% CI, 1.21- 2.82) that occurred at a younger age and was independent of metabolic syndrome and type 2 DM [3]. Furthermore, the vascular changes if develop during GDM lead to vascular diseases in women during later years of life [31]. Overall at global level hemorrhage, hypertensive disorder, obstructed labor and infection /sepsis are among the leading causes of maternal mortality, all linked to High blood pressure and hyperglycemia, directly or indirectly as leading risk factors of death by chronic condition in women.

### 3.2 Gestational Diabetes Associated Risks to the Infant

Congenital malformation risk in infants from mothers with GDM increases slightly but mostly associated with undiagnosed type 2 DM among GDM, indicating that congenital malformation are related with maternal blood glucose level, gestational age at diagnosis and maternal obesity. The patterns of congenital malformation are same as for preexisting diabetes.

Macrosomia to the fetus in women with GDM is about 20-30% and is a major risk [41]. The theory of excessive fetal insulin due to increased transport of maternal energy to the conceptus has been hypothesized among many theories which have been produced over the years to elucidate the macrosomia associated with diabetes in pregnancy [42]. Diabetes in pregnancy is associated with increased delivery of glucose and amino acids to the fetus via the maternal circulation [43]. These fuels motivate increased production of fetal insulin which promotes somatic growth. Other maternal substrates such as free fatty acids and triglycerides add to the growing supply of fetal substrate and further support excessive growth. This situation also falls under the goal of management of pregnancies risk factor. Some mothers who appear to have optimal metabolic control still give birth to macrosomic infants [44]. Furthermore, macrosomia is not limited to the diabetic population; in fact, approximately 25% of macrosomic infants are born to mothers without GDM. It has recently been shown that women may have glucose level within target range yet there is superfluous shunting of glucose to the fetus as confirmed by increased amniotic fluid insulin levels which are thought to be best predictor of macrosomia and decisions about

treatment therapy in the mother are based on this evidence of fetal hyper insulinemia [45] In search of the effects of intrauterine contact on adiposity and blood pressure at three years of age (n=1238) adiposity assessed by skin fold measures was found to be higher in offspring of women with GDM compared to offspring of women without GDM [12].

The frequency of neonatal complications varies from 12-28% with aggressive management of GDM and the commencement of screening [46]. Macrosomia increased the danger of requiring a cesarean section of mother and place the infant at risk of shoulder dystocia. It is reported in a randomized trial that insulin therapy in women with GDM can decrease the rate of fetal macrosomia in those women whose maternal glucoses are at target levels on diet alone but whose fetuses showed excessive growth [47]. Shoulder dystocia can result in Erb's palsy, clavicular fractures, fetal distress, low APGAR scores, and even birth asphyxia while unrecognized [48]. Shoulder dystocia occurs nearly 50% of the time when a 4500 gram infant is delivered vaginally [49]. Preterm labor can result due to polyhydramnios from the fetus because of ultra-filtrating glucose through the kidneys. In mothers who have poor glycemic control, respiratory distress syndrome may occur in up to 31% of infants while cardiac septal hypertrophy may be seen in 35- 40 % [46]. There is also an increased risk of fetal mortality due to fetal acidemia and hypoxia with extremely poor glucose control. Common metabolic abnormalities in the infant of a GDM mother, consist of neonatal hypoglycemia, is common in women in suboptimal glycemic control because the infant may continue to produce excessive insulin for up to 24 hours after birth before the normal feedback loop starts operating. An estimated fetal weight of >4500 grams carries much higher risk of shoulder dystocia and an elective cesarean section is usually recommended [46]. Women with good dating criteria, a favorable cervix, and an estimated fetal weight <4000 grams are often electively induced at 38- 39 weeks in an attempt to decrease macrosomic births [50].

#### **4. Long Term Consequences for the Risk of NCDs in the Offspring**

The long-term squeals of GDM for offspring are debatable. Reports of an increased risk of adolescent obesity and Type 2 diabetes are compelling. It is reported that fetal islet hyperplasia occurs in-utero with maternal hyperglycemia resulting in an increased risk of developing Type 2 diabetes in teenage years or as a young adult [51]. In Pima Indians, the incidence of childhood Type 2 DM at 10-14 years in the offspring of GDM mother is higher of non-diabetic mothers and 5-fold higher than that of pre-diabetic mothers who develop Type 2 DM after pregnancy has been reported [52]. Elevated amniotic fluid insulin levels (due to fetal hyper-insulinemia as a result of maternal hyperglycemia) predicted teenage obesity in one study, independent of fetal weight, and one-third of these offspring had impaired glucose tolerance by 17 years of age [53]. This situation creates massive likelihood for the incidence of Type 2DM on these children with impaired glucose tolerance especially those females become mothers themselves in future, disseminating the cycle.

A longitudinal cohort study compared the development of metabolic syndrome in four groups of children 6-11 years old; these were large for gestational age offspring and appropriate for gestational age offspring of mothers with GDM, with similar offspring of control mothers. The observation of the study showed that large for gestational age offspring of GDM mothers represent a higher prevalence of developing the metabolic syndrome (50%), compared to offspring of the other 3 groups. It has also estimated in the same study that 5-7 year old children of mothers with GDM have increased prevalence of obesity and metabolic syndrome, especially when they are heavier at birth [54]. Further the large for gestational age offspring of the same study were at an increased risk of developing insulin resistance. The odds ratio of developing diabetes in children of mothers with gestational diabetes was 7.46 (CI 4.85 - 11.50) compared with development of diabetes in children of mothers without GDM [54]. Further, observations in a small cohort of children (average age 9 years) of a low risk Caucasian population, showed that offspring of mothers with GDM were at an increased risk of developing glucose intolerance [55]. Similar observations have been reported in a multi-ethnic population, the odds of having type 2 DM was 5.7 (CI 2.4-13.4) after exposure to maternal GDM in utero [56].

There are some likely biological mechanisms through which GDM increases the risk of an offspring to have obesity or DM. In the early phase of intrauterine development of the fetus in women with GDM, there is increased vulnerability of having a defect in organogenesis and physiologic function development when exposed to increased levels of metabolic substrates, such as amino acids, glucose and fatty acids, Moreover IUGR in a female fetus can also result in women having GDM as adults [34], [57].

#### **5. Solution**

Diabetic pregnancy was associated with high maternal and fetal mortality before the discovery of insulin. The perinatal mortality was 50% before and has reduced to 2-5% at the present time after the discovery of insulin. Further, we support the previous suggestions that after fetal lung maturity confirmation by amniocentesis, an earlier delivery should be considered in women with GDM who require insulin or glyburide or those who are not taking insulin but have suboptimal glycemic control, and should undergo fetal surveillance at 32 weeks gestation [34]. Similarly an ultrasound for growth to look for head to body disproportion and evidence at 28-32 weeks would influence treatment [47]. Ultrasonography can often envisage the risk of fetal macrosomia by measuring the abdominal circumference of the fetus at 29-33 weeks.

Applications of careful regulation of maternal glycaemia giving benefits to fetus have been accepted but the question of intrauterine deaths and congenital malformations is quiet there. It is suggested that chronic intrauterine hypoxia leading to acidemia is the most likely cause of still birth. In the past, the congenital anomalies were responsible for 10 % of all perinatal deaths. At present, they account for 30-50 %

of perinatal mortality. Currently it's thought that derangement in maternal glycaemia possibly in association with genetic susceptibility and epigenetic changes contributes to abnormal embryogenesis.

There is a need to work at two levels in this high risk population in low income countries such as Pakistan, with increasing trend of diabetes and other chronic diseases, such as in Pakistan other low income countries. One is to prevent the development of GDM and the other is to organize program for reducing the incidence of type 2 DM. In agreement with a prospective cohort study reported from Karachi showing that increased BMI, increased body fat percentage, decreased physical activity levels and diet are autonomous adjustable interpreters of GDM [2]. Therefore it is suggested that prevention programs and health care system along with the resources such as directing for improved physical activity levels, reducing weight and improving diet in women of reproductive age may be helpful to overcome the consequences of GDM.

Further high BMI values and post-partum impaired glucose tolerance of women are strong clinical indicators for type 2 DM in women with GDM. Postpartum screening of women with GDM should assess cholesterol and lipoprotein levels, plasma glucose and BMI measurements in women to establish a rigorous lifestyle plan, which should include diet and physical activity to prevent development of GDM in subsequent pregnancies, as well as type 2 DM and metabolic syndrome later in life. Awareness of the women with regard to the threat of type 2 DM after GDM should be increased. We reemphasize the previously suggested ways of several studies [49] that better maternal education of women with a history of GDM should be introduced. The best time for motivating and educating women is during pregnancy so that they carry it further during the postpartum period to delay development of diabetes and recurrent GDM.

For implementing these suggestions the role of health professionals is of tremendous importance. They have a responsibility towards the society to ensure better health and reduction in diseases related events in individuals at higher risk. At present, there are no standard guidelines for prevention and treatment of GDM in Pakistan. There is an immense need for developing them to address this important health area.

## 6. Conclusion

GDM can have serious immediate as well as long term implications for the health of the mother as well as the offspring. Diabetes situation is different in terms of the scale, type of problem and health care system dealing with problem. In Pakistan the prevalence rate of type 2 DM has been projected to rise in the future. Preventive strategies as life style modifications such a healthy diet, losing weight, quit smoking and healthy physical activity will reduce the rate of obesity and hypertension which in turn will go a long way in decreasing the rising incidence of Type 2 Diabetes Mellitus.

## References

- [1] A. Aberg, H. Rydhstroem, A. Frid. Impaired glucose tolerance associated with adverse pregnancy outcome: A population based study in Southern Sweden. *Am J Obstet Gynecol*,184, pp 77-83, 2001.
- [2] R. Iqbal, G. Rafique, S. Badruddin, R. Qureshi, R. Cue, K. Gray-Donald. "Increased body fat percentage and physical inactivity are independent predictors of gestational diabetes mellitus in South Asian women". *Eur J Clin Nutr*, 61, pp 736-42, 2007.
- [3] D.B. Carr, K.M. Utzschneider, R.L. Hull, J Tong, T.M. Wallace, K Kodamal. "Gestational diabetes mellitus increases the risk of cardiovascular disease in women with a family history of type 2 diabetes". *Diabetes Care*, 29, pp2078-83, 2006.
- [4] M.M. Hedderson, J.A. Darbinian, A. Ferrara. "Disparities in the risk of gestational diabetes by race-ethnicity and country of birth". *Paediatric and perinatal Epidemiology*, 24(5), pp. 441-8, 2010.
- [5] Expert committee on the diagnosis and classification of Diabetes Mellitus: Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 26(Supp. 1) 55, 520-590, 2004
- [6] A. Ferrara. "Increasing prevalence of GDM, *Diabetes Care*, 3 (2), ppS141-6, 2007.
- [7] American College of Obstetrics and Gynecologists Committee on Practice Bulletins-Obstetrics: Gestational diabetes. Number 30, September 2001. *Obstet. Gynecol*, 98, pp 525-38, 2001
- [8] American Diabetes Association: "Gestational diabetes mellitus (Position Statement)". *Diabetes Care*,27, pp S88-S90, 2004.
- [9] C.D. Naylor, D. Phil, M. Sermer, E. Chen, D. Farine. "Selective screening for gestational diabetes mellitus". *N Engl J Med*, 337, pp 1591-96, 1997
- [10] L. Haakova, D. Cibula, K. Rezabek, M. Hill, M. Fanta, J. Zivny. "Pregnancy outcome in women with PCOS and in controls matched by age and weight". *Hum Reprod*,18, pp 1438-41, 2003.
- [11] S. Bjercke, P.O. Dale, T. Tanbo, R. Storeng, G. Ertzeid, T. Abyholm." Impact of insulin resistance on pregnancy complications and outcome in women with polycystic ovary syndrome". *Gynecol Obstet Invest*,54,pp 94-98, 2002.
- [12] S.C. Brody, R. Harris, K. Lohr. "Screening for gestational diabetes: a summary of the evidence for the U.S. Preventive Services Task Force". *Obstet Gynecol*, 101,pp 380-92, 2003.
- [13] M.W. Carpenter, D.R. Coustan. "Criteria for screening tests for gestational diabetes". *Am J Obstet Gynecol*,144,pp 768-73, 1982.
- [14] L. Tracy, N Mark. M.D. Feinglos. "Gestational Diabetes Mellitus". *Clinical Diabetes*. 23, pp17-24, 2005.
- [15] I.M. Evers, H.W. de Valk, G.H. Visser. "Risk of complications of pregnancy in women with type 1 diabetes: nationwide prospective study in the Netherlands". *BMJ*,pp328:915, 2004.
- [16] G.D. Cianni, R. Miccoli, L. Volpe, C Lencioni, S Del Prato "Intermediate metabolism in normal pregnancy



- and in gestational diabetes". *Diabetes Metab Res Rev*, 19, pp 259-70, 2003.
- [17] A.H. Xiang, R.K. Peters, E. Trigo, S.L. Kjos, W.P. Lee, T.A. Buchanan "Multiple metabolic defects during late pregnancy in women at high risk for type 2 diabetes". *Diabetes*, 48, pp 848-54, 1999.
- [18] D. Maurico, M. Balsells, J. Morales, R. Corcoy, M. Puig-Domingo, A. de Leiva "Islet cell autoimmunity in women with gestational diabetes and risk of progression to insulin-dependent diabetes mellitus". *Diabetes Metab Rev*, 12, pp 275-85, 1996.
- [19] C. Rosemary, J. Vivien, R. Helen. "Prepregnancy Care and Pregnancy Outcomes in Women with Type 1 Diabetes". *Diabetes Care*, 29, pp 1744-49, 2006
- [20] R. Temple, V. Aldridge, R. Greenwood, P. Heyburn, M. Sampson, K. Stanley "Association between outcome of pregnancy and glycaemic control in early pregnancy in type 1 diabetes: population based study". *BMJ*, 32, pp. 1275-76, 2002.
- [21] J.L. Kitzmiller, L.A. Gavin, G.D. Gin, L. Jovanovic-Peterson, E.K. Main, W.D. Zigrang "Preconception care of diabetes: glycemic control prevents congenital anomalies". *JAMA*, 265, pp. 731-36, 1991
- [22] J.L. Mills, L. Baker, A.S. Goldman. "Malformations in infants of diabetic mothers occur before the seventh gestational week: implications for treatment". *Diabetes*, 28, pp. 292-93, 1979.
- [23] J.G. Ray, T.E. O'Brien, W.S. Chan. "Preconception care and the risk of congenital anomalies in the offspring of women with diabetes mellitus: a meta-analysis". *QJM*, 94, pp 435-44, 2001.
- [24] J. G. Ray, M.J. Vermeulen, J.L. Shapiro, A.B. Kenshole. "Maternal and neonatal outcomes in pregestational and gestational diabetes mellitus and the influence of maternal obesity and weight gain: the DEPOSIT\* study". *Q J Med*, 94, pp. 347-56, 2001
- [25] C.D. Naylor, M. Sermer, E. Chen, K. Sykora. "Cesarean delivery in relation to birth weight and gestational glucose tolerance". *JAMA*, 275, pp. 1165-70, 1996
- [26] E.C. Kieffer, G.R. Alexander, M.D. Kogan, J.H. Nimes. "Influence of diabetes during pregnancy on gestational age-specific newborn weight among US black and US white infants". *Am J Epidemiol* 147, pp. 1053-61, 1998
- [27] M. Godwin, M. Muirhead, J. Huynh, B. Helt, J. Grimmer. "Prevalence of gestational diabetes mellitus among Swampy Cree women in Moose Factory, James Bay". *CMAJ*; 160, pp. 1299-1302, 1999
- [28] L.L. Moore , M.R. Singer, M.A. Loring Bradlee "Prospective study of the risk of congenital defects associated with maternal obesity and diabetes mellitus". *Epidemiology*;11, pp. 689-94, 2000
- [29] S.C. Brody, R. Harris, K. Lohr "Screening for gestational diabetes: A summary of the evidence for the U.S. Preventive Services Task Force". *Obstet Gynecol*, 101, pp. 380-92, 2003.
- [30] F.G. Cunningham, N. F. Gant, K. J. Leveno, et al. "Diabetes," in *Williams Obstetrics*, F.G Cunningham, N.F Gant, K. J Leveno (21<sup>st</sup> ed.) McGraw-Hill, New York, 2001.
- [31] S.R Carr. "Screening for gestational diabetes mellitus. A perspective in 1998" *Diabetes Care*, 21 (2), pp. B14-8, 1998.
- [32] X. Xiong, L.D Saunders, F.L Wang, N.N Demianczuk, "Gestational diabetes mellitus: prevalence, risk factors, maternal and infant outcomes," *Int J Gynaecol Obstet*, 75, pp. 221-8, 2001
- [33] A.K. Shefali, M. Kavitha, R. Deepa, V. Mohan, "Pregnancy outcomes in pre-gestational and gestational diabetic women in comparison to non-diabetic women-- A prospective study in Asian Indian mothers", *J Assoc Physicians India*, 54, pp. 613-8, 2006.
- [34] F.A Van Assche, K. Holemans, L. Aerts "Long-term consequences for offspring of diabetes during pregnancy". *Br Med Bull*, 60, pp. 73-82, 2001.
- [35] S.D. Kale, C.S. Yajnik, S.R Kulkarni, K. Meenakumari, A.A. Joglekar, N. Khorsand, et al. "High risk of diabetes and metabolic syndrome in Indian women with gestational diabetes mellitus", *Diabet Med*, 21, pp. 1257-8, 2004.
- [36] N. Sattar, I.A Greer. "Pregnancy complications and maternal cardiovascular risk: opportunities for intervention and screening," *BMJ*, 325, pp. 157-60, 2002.
- [37] J. Lauenborg, T. Hansen, D.M. Jensen, H. Vestergaard, P.L. Molsted, P. Hornnes, et al. "Increasing incidence of diabetes after gestational diabetes: a long-term follow-up in a Danish population," *Diabetes Care*, 27, pp. 1194-1199, 2004.
- [38] J. Lauenborg, E. Mathiesen, T. Hansen, C. Glumer, T. Jorgensen, K. Borch-Johnsen, et al. "The prevalence of the metabolic syndrome in a Danish population of women with previous gestational diabetes mellitus is three-fold higher than in the general population", *J Clin Endocrinol Metab* 90, pp. 4004-4010, 2005.
- [39] B. Sinha, P. Brydon, R.S. Taylor, A. Hollins, A. Munro, D. Jenkins, et al. "Maternal ante-natal parameters as predictors of persistent postnatal glucose intolerance: a comparative study between Afro-Caribbeans, Asians and Caucasians," *Diabet Med*, 20, pp. 382-386, 2003.
- [40] M.M. Hedderon, A. Ferrara, D.A. Sacks. "Gestational diabetes mellitus and lesser degrees of pregnancy hyperglycemia: association with increased risk of spontaneous preterm birth," *Obstet Gynecol*, 102, pp. 850-856, 2003.
- [41] A. L Kjos, T.A. Buchanan, "Gestational diabetes mellitus, *N Engl J Med*, 341, pp. 1749-1756, 1999.
- [42] E.A. Reece, C.J. Homko, "Why do diabetic women deliver malformed infants?" *Clinical Obstet Gynecol*, 43, pp. 32-45, 2000.
- [43] K. Gaither, A.N. Quraishi, N.P. Illsley, "Diabetes alters the expression and activity of the human placental GLUT1 glucose transporter," *J Din Endocrinol Metabol*, 84, pp. 695-701. 1999.
- [44] M.S Magee, C.E Walden, T.J Benedetti, R.H Knopp, "Influence of diagnostic criteria on the incidence of gestational diabetes and perinatal morbidity" *JAMA* 269, pp. 609-15. 1993.
- [45] A.M. Weiss, H.S. Scholz, J.H. Haas, K.F. Tamussino, "Effect of fetal hyperinsulinemia on oral glucose tolerance test results in patients with gestational diabetes mellitus," *Am J Obstet Gynecol*, 184, pp. 470-5, 2001.
- [46] M.B. Landon, "Obstetric management of pregnancies complicated by diabetes mellitus," *Clinical Obstet Gynecol*, 43, pp. 65-74. 2000.

- [47] T.A. Buchanan, S.I. Kjos, M.N. Montoro, "Use of fetal ultrasound to select metabolic therapy for pregnancies complicated by mild gestational diabetes," *Diabetes Care*, 17, pp. 275-83, 1994.
- [48] O. Langer, "Management of gestational diabetes," *Clinical Obstet Gynecol*, 43, pp. 106-115, 2000.
- [49] D.L. Conway. "Elective delivery of infants with macrosomia in diabetic women: reduced shoulder dystocia versus increased cesarean deliveries," *Am J Obstet Gynecol*, 178 pp. 922-925, 1998.
- [50] S.L. Kjos, "Postpartum care of the woman with diabetes," *Clinical Obstet Gynecol*, 43, pp. 75-90, 2000.
- [51] R.S. Lindsay, R.L. Hanson, P.H. Bennett, "Secular trends in birth weight, BMI, and diabetes in the offspring of diabetic mothers," *Diabetes Care*, 23 pp. 1249-1954, 2000.
- [52] D.J. Pettitt, R.G. Nelson, M.F. Saad, P.H. Bennett, W.C. Knowler, "Diabetes and obesity in the offspring of Pima Indian women with diabetes during pregnancy", *Diabetes Care* , 16, pp. 310-314, 1993.
- [53] B. L. Silverman, B. E. Metzger, "Impaired glucose tolerance in adolescent offspring of diabetic mothers," *Diabetes Care*, 18, pp. 611-617, 1995.
- [54] C.M. Boney, A. Verma, R. Tucker, B.R. Vohr, "Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus," *Pediatrics*, 115, pp. 290-296, 2005.
- [55] J.C. Malcolm, M.L. Lawson, I. Gaboury, G. Lough, E. Keely, "Glucose tolerance of offspring of mother with gestational diabetes mellitus in a low-risk population," *Diabet Med*, 23, pp. 565-570 2006.
- [56] A. Thapar, G. Harold, F. Rice, X. Ge, J. Boivin, D. Hay, et al. "Do intrauterine or genetic influences explain the foetal origins of chronic disease? A novel experimental method for disentangling effects," *BMC Med Res Method*, 7, pp. 25, 2007.

## Authors Profile

**Bushra Chaudhry** is PhD in Molecular Biology, faculty member of BBS Department and corresponding author. Asifa Alia is MBBS, FCPS, currently, an Obstetrics and Gynaecology consultant at various hospitals and collaborative researcher with Aga Khan University. Syeda Sadia Fatima is MBBS, M. Phil, currently in faculty of Physiology, BBS Department at Aga Khan University.