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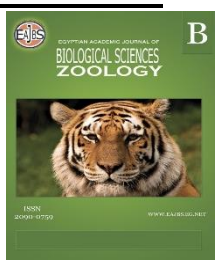

Cardiac Hypertrophy: Neonatal Pregnancy Disorder

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ABSTRACT

Cardiac hypertrophy is a chief dangerous factor for heart failure, which is the leading cause of child mortality among birth defects internationally. It is a disorder that is defined by the heart muscle thickening, which expands the size of the heart chambers to improve the heart's capacity to pump blood into the body's tissues and organs. Pregnant women with a family history, of pre-gestational diabetes mellitus (PGDM), preeclampsia, or hypertension are at high risk of carrying a fetus with cardiac hypertrophy. These inborn developmental defects might include various cardiac defects along with fetal cardiomyopathy. Symptoms of the disease vary from minor to major and may include chest pain, as well as dyspnea. It is diagnosed based on medical history, a physical exam and echocardiogram results. Protection and treatment of the unborn fetus with cardiac hypertrophy can be achieved via lifestyle adjustment, obesity avoidance, medications and sometimes procedures. The aim of the current research is to address the etiology, diagnosis, pathogenesis and protection from cardiac hypertrophy as a teratological disorder in embryo.

Contents

I. Introduction

Cardiac hypertrophy is a chief dangerous factor for heart failure, which is the leading cause of child mortality among birth defects internationally (Kumarswamy and Thum, 2013; Gelb et al., 2013). Although genomic issues contribute significantly toward root cardiac heart diseases (CHD), specific genetic lesions are unknown for patients

(Reller et al.,2008). Adult humans fail to renew their hearts after injury. This disappointment to renew the myocardium is a reason for heart disorder and death worldwide. In spite of, only adult mammals near death have a high ability to renew their heart, cardiac muscle can be regenerated throughout life in some vertebrates (Reller *et al.,* 2008).

Cardiac hypertrophy is a general response of the heart muscle towards many physiological and pathological stimuli. It has been stated that CHD is characterized by increased heart mass relative to body weight. CHD or Inflation of the heart is generally divided into two groups: adaptive and maladaptive. Adaptive inflation includes both physiological hypertrophy and compensated hypertrophy.

First, physiological hypertrophy is induced by physiological stimuli, such as pregnancy and exercise. Second, compensated hypertrophy is achieved in response to hemodynamic stress, neurohumoral stimuli and other pathological insults (Hunter and Chien, 1999; Frey and Olson, 2003). Physiological hypertrophy is characterized by increased cardiac size with regular and/or enhanced cardiac function. Especially, exercise-induced physiological hypertrophy offers significant cardioprotection toward ischemia-reperfusion injury and pressure overload insult (Powers *et al.,* 2014; Moreira-Goncalves *et al.,* 2015). If the previous harmful factors, such as dynamic stress and hyperstimulation of the neurotransmitter, continue, the compensated hypertrophy may change into maladaptive hypertrophy and lead to heart failure (Condorelli *et al.,* 2008). Cardiac hypertrophy is a disorder defined by the thickening of the heart muscle, which causes the heart chambers to enlarge, expanding the heart's ability to pump blood to tissues and organs throughout the body (Xiangbo *et al.,* 2016).

Early pregnancy is a sensitive period for fetal cardiac development, and it is possible that maternal blood pressure, or other cardiovascular alterations during pregnancy, has a direct effect on the development of offspring cardiac structures. Cardiac structures develop early in the human fetus, and by the end of the first trimester, they are largely developed and functional (Leiva *et al.,* 1999).

Neonatal cardiac hypertrophy during gestation and/or later after birth might be due to intrauterine exposure to hyperglycemia, preeclampsia, and high blood pressure (Fraser *et al.,* 2013; Davis *et al.,* 2012; Kajantie *et al.,* 2009). Women with diabetes before pregnancy are more susceptible to having children with congenital malformations, cardiac abnormalities, and nervous system disorders than non-diabetic women. These diseases occur early because both the vascular and nervous system appears to develop at an early stage, the period that is vulnerable to external harmful factors (Wickstrom *et al.,* 2005; Rich-Edwards *et al.,*2014; Jayet *et al.,*2010).

Pregnant women with either pre-gestational diabetes mellitus (PGDM) or gestational diabetes mellitus are at high susceptibility (2–5 times higher than non-diabetic pregnancies) to carrying a fetus with congenital anomalies, such as phocomelia, cardiac disturbances, macrosomia and central nervous system malformations (Ejdesjo *et al.,* 2012; Gheorman *et al.,* 2011). Among those congenital disorders induced by hyperglycemia, congenital heart disease (Simeone *et al.,* 2015) and anomalies of the nervous system are the most prominent (Li *et al.,* 2012). It was stated that both the cardiovascular and nervous systems start to develop during the early embryonic developmental stage, the period that is at risk to external harmful elements.

Hyperglycemia is hypothesized to be the most important teratogen affecting cardiovascular formation as a result of producing excess reactive oxygen species (ROS) (Zangen *et al.,* 2002; Jin *et al.,* 2013). These inborn developmental defects might include various cardiac defects along with fetal cardiomyopathy (Corrigan *et al.,* 2009). Diabetic cardiomyopathy induced principally by continuous hyperglycemia displays as cardiac

hypertrophy, and heart failure would occur if serious pathogenesis existed (Ding *et al.*, 2013).

It has been reported that Cardiac structure defects including cardiac hypertrophy in youth might be attributed to fetal exposure to preeclampsia (Simon *et al.,* 2016). In Saudi Arabia, 566 out of 2269 had neonatal congenital heart disease (Reller *et al.*, 2008).

The aim of the current research is to address the etiology, diagnosis, pathogenesis and protection from cardiac hypertrophy as a teratological disorder in embryo.

II.Etiology:

The causes of coronary artery disease are still unknown to a large extent (Reller *et al.*, 2008). It is well known that the main constituents of the embryonic heart are composed of the cardiac precursor cells, the cardiac neural crest and the pro-epicardium. During cardiogenesis, a greater risk of congenital heart disease is possible if the migration or differentiation of cardiac precursor cells is altered. For example, a change in the embryological origin of the right and left ventricular myocardium is implicated in congenital heart disease.

Another consideration is that cardiogenesis is a very complex process and that the heart is susceptible to both internal and externally damaging stimuli. Normal heart formation relies on specific spatiotemporal regulation by heart-development-related genes at different embryonic developmental stages. It has been shown that fibroblast growth factor signaling is required for the rearrangement of cardiac progenitor cells in the primary heart field of Drosophila and chicks. This cardiac precursor specification occurs when these cells reach the anterior lateral plate mesoderm (Martinsen, 2005; Zaffran *et al.,* 2004; Beiman *et al.,* 1996; Yang *et al.*, 2002). In addition, bone morphogenetic protein 2 (BMP2) expressed by the anterior endoderm is considered a crucial stimulator for the myocardium and plays an important role in cardiac induction in the chick embryo. Furthermore, Nkx2.5 and GATA4, as well as myocardin and Tbx20, are essential transcription factors that characterize and control the cardiogenic differentiation of cardiac processor cells (Ejdesjo *et al.,* 2012). The excessive production of reactive oxygen species (ROS) is one factor that is relevant to DM T2 (Diabetes Mellitus Type 2) and is responsible for the development of diabetic cardiomyopathy (Huynh *et al.,* 2012). This is achieved either through participation in the production of ROS or independent of ROS production. However, the exact pathogenesis of hyperglycemia-induced cardiac hypertrophy in a developing fetus still remains controversial.

Offspring exposed to intrauterine preeclampsia have decreased flow-mediated dilation, which was not observed in their unexposed fraternal, suggesting a direct maternal effect. Additionally, a direct effect of exposure to preeclampsia on fetal cardiac development is reasonable and is due to disturbed pressure loads and hypoxia during the development of the myocardium which might have a long-lasting impact on its structure and function. The increase in the number of myocytes in the human myocardium is obvious during early life, and subsequent cardiac growth is mostly mediated through hypertrophy of previously formed myocytes which is obvious later during adolescence as an outcome of fetal preeclampsia exposure (Simon *et al.,* 2016).

Women with preeclampsia have altered left ventricular geometry compared to those with a normal pregnancy, (Melchiorre *et al.,*2011) which only partly is reversible postpartum Melchiorre *et al.,*2011). Meanwhile, women with gestational hypertension have been found to demonstrate higher relative wall thickness (RWT), a measure of left ventricular concentricity, in late pregnancy compared to normotensive pregnant women, (Valensise *et al.,* 2001) and RWT in adolescence seems to have a substantial heritable component (Kapuku *et al.,*2008) Thus, women with altered cardiac geometry or greater RWT might be both more likely to have preeclampsia or hypertension during pregnancy,

as well as to have offspring with altered cardiac geometry and higher RWT simply because of shared genes between mother and offspring.

In the adult heart, factors that elevate blood pressure such as Angiotensin-II (ANG-II) have direct effects on cardiac function and structure, inducing several growth-promoting genes, protein synthesis, and cell growth (Sadoshima and Izumo, 1993; Schunkert *et al.,* 1995). For an instance, the renin-angiotensin system (RAS) plays a crucial role in cardiovascular control. In the mature heart, infusion of ANG II stimulates the development of cardiac hypertrophy independently of effects on blood pressure (Dostal and Baker, 1992; Kim et al., 1995), whereas blockade of the renin-angiotensin system (RAS) with a converting-enzyme inhibitor or an ANG II type 1 (AT_1)-receptor antagonist attenuates the development of pressure overload-induced hypertrophy and inhibits many of the molecular and cellular adaptations to pressure-overload states (Pan *et al.,* 1997; Rockman *et al.,* 1994). The responsiveness of the immature myocardium to pressure elevating factors is less well studied. In vitro, ANG II stimulates fetal cardiomyocyte proliferation, but not hypertrophy (Sundgren *et al.,* 2003). In vivo, infusion of ANG II results in late-gestation fetal cardiomyocyte proliferation and hypertrophy; however, whether this is a direct or indirect effect, resulting from increased blood pressure and mechanical load is not known (Norris *et al.,* 2014). It has been found that pressure risen factors significantly increased fetal mean blood pressure by 15–20 mmHg, resulting in increased cardiac mass via cardiomyocyte hypertrophy and proliferation (Norris *et al.,* 2014; Segar *et al.,* 2001). It was also demonstrated that ANG II indirectly induces cardiac growth, cardiomyocyte hypertrophy, and maturation in early-gestation fetal sheep primarily through load-dependent mechanisms.

III.Symptoms and Diagnosis:

Symptoms of the disease vary from minor to severe and may include chest pain, dyspnea. Fetal investigations show an increase in the heart mass, not only through hyperplasia, which is a process dependent on dislocation but also through the fetal stages recognized through physiological inflation, metastasis, musculoskeletal retrieval, regrowth and hypertensive growth.

Various reports indicated that no clinical uniform diagnostic standard for fetal cardiac hypertrophy. However, fetal cardiac hypertrophy in clinical cases could be confirmed if the interventricular septum (IVS) is greater than two standard deviations. The reports (Martinsen, 2005) showed that the value of normal full-term fetal IVS and left ventricular posterior wall (LVPW) was 2.4mm in a color ultrasound. Therefore, they used the value of 2.4 mm as the standard for the examination of fetal hearts using color ultrasound.

In the animal model of fetal cardiac hypertrophy, the thickness of the right ventricular anterior wall (RVAW), the thickness of IVS and the thickness of the left ventricular posterior wall (LVPW) were greater when compared with the control group. In addition, the diameters of the cardiac cavities in (right and left ventricular cavities) were less than the cardiac cavities of the control group. The vertical sections of fetal cardiac hypertrophic mice revealed the hypertrophic heart and cardiac cavity shrank in mouse hearts compared to those of the control group at the same developmental stage (Sha-shaHan *et al.,* 2015).

Noteworthy, later in offspring, cardiac hypertrophy is diagnosed based on medical history (your symptoms and family history), a physical exam, and echocardiogram results. Additional tests may include blood tests, electrocardiogram, chest X-ray, exercise stress test, cardiac catheterization, CT scan, and MRI (https://www.webmd.com/heart-disease/guide/hypertrophic-cardiomyopathy#1).

IV. Pathogenesis:

IV. 1. Cardiac Hypertrophy And Diabetes:

Alterations in cell magnitude rather than cell proliferation or apoptosis are responsible for hyperglycemia-induced fetal cardiac hypertrophy, and its regulatory target genes in the presence of high glucose could be a principal component of pathogenesis in the education of fetal cardiac hypertrophy (Ejdesjo *et al.,* 2012), early growth and subsequent risk of diseases including obesity, DM T2, and ischemic heart disease (Blackmore and Ozanne, 2015; Cosmi *et al.,* 2014; Kanguru *et al.,* 2014).

Pregestational diabetes is the leading cause of fetal intrauterine growth retardation. It is well known that a pregnant woman with DM T2 and her unborn child are equally at bigger risk of gestation complications such as pre-eclampsia, preterm births, stillbirths, macrosomia, miscarriage, growth retardation, and congenital anomalies (Bhat *et al.,* 2012; Yogev *et al.,* 2010; Somaratne *et al.,* 2011). Cardiac septal overgrowth effects on neonates born to mothers with pregestational diabetes. The functional impact of neonatal cardiac septal hypertrophy can range from clinically asymptomatic to potentially fatal congestive heart failure stemming from left ventricular Channel obstruction (Aman *et al.,* 2011; Gutgesell and Speer, 2980).

IV. 2. Cardiac Hypertrophy in Relation to Preeclampsia and High Blood Pressure:

Shared genetic risk between the mother and offspring may thus be a contributor to increased offspring risk. However, offspring exposed to maternal preeclampsia have decreased flow-mediated dilation, which was not observed in their unexposed siblings, suggesting a direct intrauterine effect (Jayet *et al.,* 2010).

Furthermore, a direct influence of exposure to preeclampsia on fetal cardiac development is plausible (Lewandowski and Leeson, 2014), given that altered pressure loads and hypoxia during the development of the myocardium might have a long-lasting effect on its structure and function (Davis *et al.,* 2012; Kehat and Molkentin, 2010). The increase in the number of myocytes in the human myocardium plateaus during early life and subsequent cardiac growth is mostly mediated through hypertrophy of previously formed myocytes (Anversa *et al.,* 2007).

Several but not all, studies have suggested that exposure to maternal preeclampsia or hypertension during pregnancy is associated with adverse cardiac or vascular structure and function in offspring in childhood (Jayet *et al.,* 2010; Fugelseth *et al.,* 2011; Himmelmann *et al.,* 1994; Kvehaugen *et al.,* 2011) and later in life (Lewandowski *et al.,* 2013).

V. Protection and Treatment:

Unfortunately, prolonged cardiac hypertrophy finally leads to heart failure and death. Even with normal cardiac function in the early period of cardiac hypertrophy, the cardiomyocytes undergo phenotypic changes such as increased cell magnitude, although large efforts have been made to unravel the molecular mechanism underlying the changes that occur during cardiac hypertrophy and heart failure, the molecular mechanisms remain elusive. (Simon *et al.,* 2016; Reller *et al.,* 2008; Martinsen, 2005).

Treatment for children who are born with cardiac hypertrophy is intended at avoiding symptoms and complications and involves risk identification and regular follow-up, lifestyle adjustment, medications, and surgical procedures if necessary.

Diet, drinking at least six to eight, 8-ounce glasses of water a day is important unless fluids are restricted. Most people with cardiomyopathy are able to do non-competitive aerobic exercise. However, they may be asked not to do exercise, based on their symptoms and the severity of the disease. Heavy weight lifting is not recommended. Patients with Hypertrophic cardiomyopathy (HCM) should have an annual follow-up visit with their cardiologist to monitor their condition.

Medications are used to relax the heart and reduce the degree of obstruction so the heart can pump more efficiently.

Surgical procedures such as septal myectomy are needed. It aims to decrease the thickened heart septal wall to widen the path for blood from the left ventricle to aorta (https://www.webmd.com/heart-disease/guide/hypertrophic-cardiomyopathy#1).

VI. Conclusion:

In conclusion, cardiac hypertrophy is a serious disorder that causes the heart muscle to thicken and the heart chambers to enlarge, increasing the heart's capacity to pump blood to the body's tissues and organs.

The exact pathogenesis of cardiac hypertrophy in a developing fetus still remains controversial. Signs of the disease vary from minor to severe symptoms. It is diagnosed later in offspring based on medical history, and echocardiogram results. Protection and treatment vary from lifestyle adjustment to medication, and surgery.

REFERENCES

Aman, J., Hansson, U., Ostlund, I., Wall, K., & Persson, B. (2011). Increased fat mass and cardiac septal hypertrophy in newborn infants of mothers with well-controlled diabetes during pregnancy. *Journal of Neonatology,* 100(2), 147–154.

An, X., Wang, J., Li, H., Lu, Z., Bai, Y., Xiao, H., Zhang, Y., & Song, Y. (2016). Speckle Tracking Based Strain Analysis Is Sensitive for Early Detection of Pathological Cardiac Hypertrophy. *PloS one,* 11(2), e0149155.

Anversa, P., Leri, A., Rota, M., Hosoda, T., Bearzi, C., Urbanek, K., Kajstura, J., & Bolli, R. (2007). Concise review: stem cells, myocardial regeneration, and methodological artifacts.*Journal of Stem cells (Dayton, Ohio),* 25(3), 589–601.

Beiman, M., Shilo, B. Z., & Volk, T. (1996). Heartless, a Drosophila FGF receptor homolog, is essential for cell migration and establishment of several mesodermal lineages. *Genes & development,* 10(23), 2993–3002.

Bhat, M., Ramesha, K. N., Sarma, S. P., Menon, S., & Ganesh Kumar, S. (2012). Outcome of gestational diabetes mellitus from a tertiary referral center in South India: a case-control study. *Journal of obstetrics and gynaecology of India,* 62(6), 644–649.

Blackmore, H. L., & Ozanne, S. E. (2015). Programming of cardiovascular disease across the life-course. *Journal of molecular and cellular cardiology,* 83, 122–130.

Condorelli, G., Latronico, M. V., & Condorelli, M. (2008). State-of-the-Art Prevention of Heart Failure: Maladaptive versus Adaptive Hypertrophy. *Heart failure monitor,* 5(4), 112–118.

Corrigan, N., Brazil, D. P., & McAuliffe, F. (2009). Fetal cardiac effects of maternal hyperglycemia during pregnancy. *Birth defects research. Part A, Clinical and molecular teratology,* 85(6), 523–530.

Davis, E. F., Lazdam, M., Lewandowski, A. J., Worton, S. A., Kelly, B., Kenworthy, Y., Adwani, S., Wilkinson, A. R., McCormick, K., Sargent, I., Redman, C., & Leeson, P. (2012). Cardiovascular risk factors in children and young adults born to preeclamptic pregnancies: a systematic review. *Pediatrics,* 129(6), e1552–e1561.

Davis, E. F., Newton, L., Lewandowski, A. J., Lazdam, M., Kelly, B. A., Kyriakou, T., & Leeson, P. (2012). Pre-eclampsia and offspring cardiovascular health: mechanistic insights from experimental studies. *Journal of Clinical science (London, England : 1979),* 123(2), 53–72.

Ding, F., Yu, L., Wang, M., Xu, S., Xia, Q., & Fu, G. (2013). O-GlcNAcylation involvement in high glucose-induced cardiac hypertrophy via ERK1/2 and cyclin D2. *Amino acids,* 45(2), 339–349.

Dostal, D. E., & Baker, K. M. (1992). Angiotensin II stimulation of left ventricular hypertrophy in adult rat heart. Mediation by the AT1 receptor. *American journal of hypertension,* 5(5 Pt 1), 276–280.

Ejdesjö, A., Wentzel, P., & Eriksson, U. J. (2012). Influence of maternal metabolism and parental genetics on fetal maldevelopment in diabetic rat pregnancy. American journal of physiology. *Endocrinology and metabolism,* 302(10), E1198–E1209.

Ejdesjö, A., Wentzel, P., & Eriksson, U. J. (2012). Influence of maternal metabolism and parental genetics on fetal maldevelopment in diabetic rat pregnancy. American journal of physiology. *Endocrinology and metabolism,* 302(10), E1198–E1209.

Ejdesjö, A., Wentzel, P., & Eriksson, U. J. (2012). Influence of maternal metabolism and parental genetics on fetal maldevelopment in diabetic rat pregnancy. American journal of physiology. *Endocrinology and metabolism,* 302(10), E1198–E1209.

Fraser, A., Nelson, S. M., Macdonald-Wallis, C., Sattar, N., & Lawlor, D. A. (2013). Hypertensive disorders of pregnancy and cardiometabolic health in adolescent offspring. *Hypertension (Dallas, Tex.: 1979),* 62(3), 614–620.

Frey, N., & Olson, E. N. (2003). Cardiac hypertrophy: the good, the bad, and the ugly. *Annual review of physiology,* 65, 45–79.

Fugelseth, D., Ramstad, H. B., Kvehaugen, A. S., Nestaas, E., Støylen, A., & Staff, A. C. (2011). Myocardial function in offspring 5-8years after pregnancy complicated by preeclampsia. *Journal of Early human development,* 87(8), 531–535.

Gelb, B., Brueckner, M., Chung, W., Goldmuntz, E., Kaltman, J., Kaski, J. P., Kim, R., Kline, J., Mercer-Rosa, L., Porter, G., Roberts, A., Rosenberg, E., Seiden, H., Seidman, C., Sleeper, L., Tennstedt, S., Kaltman, J., Schramm, C., Burns, K., … Rosenberg, E. (2013). The Congenital Heart Disease Genetic Network Study: rationale, design, and early results. *Journal of Circulation research,* 112(4), 698–706.

Gheorman, L., Iliescu, D., Ceauşu, I., Paulescu, D., Pleşea, I. E., & Gheorman, V. (2011). Importance of early complex evaluation in high-risk pregnancy associated to diabetes mellitus. Case presentation and review of the literature. *Romanian journal of morphology and embryology = Revue roumaine de morphologie et embryologie,* 52(3 Suppl), 1127–1132.

Gutgesell, H. P., Speer, M. E., & Rosenberg, H. S. (1980). Characterization of the cardiomyopathy in infants of diabetic mothers. *Journal of Circulation,* 61(2), 441–450.

Han, S. S., Wang, G., Jin, Y., Ma, Z. L., Jia, W. J., Wu, X., Wang, X. Y., He, M. Y., Cheng, X., Li, W. J., Yang, X., & Liu, G. S. (2015). Investigating the Mechanism of Hyperglycemia-Induced Fetal Cardiac Hypertrophy. *Journal of PloS one,* 10(9), e0139141.

Himmelmann, A., Svensson, A., & Hansson, L. (1994). Five-year follow-up of blood pressure and left ventricular mass in children with different maternal histories of hypertension: the Hypertension in Pregnancy Offspring Study. *Journal of hypertension,* 12(1), 89–95.https://www.webmd.com/heart-disease/ guide/ hypertrophic-cardiomyopathy#1.

Hunter, J. J., & Chien, K. R. (1999). Signaling pathways for cardiac hypertrophy and failure. *The New England journal of medicine,* 341(17), 1276–1283.

Huynh, K., Kiriazis, H., Du, X. J., Love, J. E., Jandeleit-Dahm, K. A., Forbes, J. M., McMullen, J. R., & Ritchie, R. H. (2012). Coenzyme Q10 attenuates diastolic

dysfunction, cardiomyocyte hypertrophy and cardiac fibrosis in the db/db mouse model of type 2 diabetes. *Journal of Diabetologia*, 55(5), 1544–1553.

Jayet, P. Y., Rimoldi, S. F., Stuber, T., Salmòn, C. S., Hutter, D., Rexhaj, E., Thalmann, S., Schwab, M., Turini, P., Sartori-Cucchia, C., Nicod, P., Villena, M., Allemann, Y., Scherrer, U., & Sartori, C. (2010). Pulmonary and systemic vascular dysfunction in young offspring of mothers with preeclampsia. *Journal of Circulation*, 122(5), 488–494.

Jayet, P. Y., Rimoldi, S. F., Stuber, T., Salmòn, C. S., Hutter, D., Rexhaj, E., Thalmann, S., Schwab, M., Turini, P., Sartori-Cucchia, C., Nicod, P., Villena, M., Allemann, Y., Scherrer, U., & Sartori, C. (2010). Pulmonary and systemic vascular dysfunction in young offspring of mothers with preeclampsia. *Journal of Circulation*, 122(5), 488–494.

Jin, Y. M., Zhao, S. Z., Zhang, Z. L., Chen, Y., Cheng, X., Chuai, M., Liu, G. S., Lee, K. K., & Yang, X. (2013). High glucose level induces cardiovascular dysplasia during early diabetes:elopment. *Experimental and clinical endocrinology & diabetes: official journal, German Society of Endocrinology [and] German Diabetes Association*, 121(8), 448–454.

Kajantie, E., Eriksson, J. G., Osmond, C., Thornburg, K., & Barker, D. J. (2009). Pre-eclampsia is associated with increased risk of stroke in the adult offspring: the Helsinki birth cohort study. *Journal of Stroke*, 40(4), 1176–1180.

Kanguru, L., Bezawada, N., Hussein, J., & Bell, J. (2014). The burden of diabetes mellitus during pregnancy in low- and middle-income countries: a systematic review. *Journal of Global health action*, 7, 23987.

Kapuku, G. K., Ge, D., Vemulapalli, S., Harshfield, G. A., Treiber, F. A., & Snieder, H. (2008). Change of genetic determinants of left ventricular structure in adolescence: longitudinal evidence from the Georgia cardiovascular twin study. *American journal of hypertension*, 21(7), 799–805.

Kehat, I., & Molkentin, J. D. (2010). Molecular pathways underlying cardiac remodeling during pathophysiological stimulation. *Journal of Circulation*, 122(25), 2727–2735.

Kim, S., Ohta, K., Hamaguchi, A., Yukimura, T., Miura, K., & Iwao, H. (1995). Angiotensin II induces cardiac phenotypic modulation and remodeling in vivo in rats. *Journal of Hypertension (Dallas, Tex. : 1979)*, 25(6), 1252–1259.

Kumarswamy, R., & Thum, T. (2013). Non-coding RNAs in cardiac remodeling and heart failure. *Journal of Circulation research*, 113(6), 676–689.

Kvehaugen, A. S., Dechend, R., Ramstad, H. B., Troisi, R., Fugelseth, D., & Staff, A. C. (2011). Endothelial function and circulating biomarkers are disturbed in women and children after preeclampsia. *Journal of Hypertension (Dallas, Tex. : 1979)*, 58(1), 63–69.

Leiva, M. C., Tolosa, J. E., Binotto, C. N., Weiner, S., Huppert, L., Denis, A. L., & Huhta, J. C. (1999). Fetal cardiac development and hemodynamics in the first trimester. *Ultrasound in obstetrics & gynecology: the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*, 14(3), 169–174.

Lewandowski, A. J., & Leeson, P. (2014). Preeclampsia, prematurity and cardiovascular health in adult life. *Journal of Early human development*, 90(11), 725–729.

Lewandowski, A. J., Augustine, D., Lamata, P., Davis, E. F., Lazdam, M., Francis, J., McCormick, K., Wilkinson, A. R., Singhal, A., Lucas, A., Smith, N. P., Neubauer, S., & Leeson, P. (2013). Preterm heart in adult life: cardiovascular

magnetic resonance reveals distinct differences in left ventricular mass, geometry, and function. *Journal of Circulation,* 127(2), 197–206.

Li, X., Weng, H., Xu, C., Reece, E. A., & Yang, P. (2012). Oxidative stress-induced JNK1/2 activation triggers proapoptotic signaling and apoptosis that leads to diabetic embryopathy. *Diabetes,* 61(8), 2084–2092.

Martinsen B. J. (2005). Reference guide to the stages of chick heart embryology. *Developmental dynamics: an official publication of the American Association of Anatomists,* 233(4), 1217–1237.

Melchiorre, K., Sutherland, G. R., Baltabaeva, A., Liberati, M., & Thilaganathan, B. (2011). Maternal cardiac dysfunction and remodeling in women with preeclampsia at term. *Journal of Hypertension (Dallas, Tex. : 1979),* 57(1), 85–93.

Melchiorre, K., Sutherland, G. R., Liberati, M., & Thilaganathan, B. (2011). Preeclampsia is associated with persistent postpartum cardiovascular impairment. *Journal of Hypertension (Dallas, Tex. : 1979),* 58(4), 709–715.

Moreira-Gonçalves, D., Henriques-Coelho, T., Fonseca, H., Ferreira, R., Padrão, A. I., Santa, C., Vieira, S., Silva, A. F., Amado, F., Leite-Moreira, A., & Duarte, J. A. (2015). Intermittent cardiac overload results in adaptive hypertrophy and provides protection against left ventricular acute pressure overload insult. *The Journal of physiology,* 593(17), 3885–3897.

Norris, A. W., Bahr, T. M., Scholz, T. D., Peterson, E. S., Volk, K. A., & Segar, J. L. (2014). Angiotensin II-induced cardiovascular load regulates cardiac remodeling and related gene expression in late-gestation fetal sheep. *The Journal of Pediatric research,* 75(6), 689–696.

Pan, J., Fukuda, K., Kodama, H., Makino, S., Takahashi, T., Sano, M., Hori, S., & Ogawa, S. (1997). Role of angiotensin II in activation of the JAK/STAT pathway induced by acute pressure overload in the rat heart. *Journal of Circulation research,* 81(4), 611–617.

Powers, S. K., Smuder, A. J., Kavazis, A. N., & Quindry, J. C. (2014). Mechanisms of exercise-induced cardioprotection. *Physiology (Bethesda, Md.),* 29(1), 27–38.

Reller, M. D., Strickland, M. J., Riehle-Colarusso, T., Mahle, W. T., & Correa, A. (2008). Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. *The Journal of pediatrics,* 153(6), 807–813.

Reller, M. D., Strickland, M. J., Riehle-Colarusso, T., Mahle, W. T., & Correa, A. (2008). Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. *The Journal of pediatrics,* 153(6), 807–813.

Rich-Edwards, J. W., Fraser, A., Lawlor, D. A., & Catov, J. M. (2014). Pregnancy characteristics and women's future cardiovascular health: an underused opportunity to improve women's health?. *Epidemiologic reviews,* 36(1), 57–70.

Rockman, H. A., Wachhorst, S. P., Mao, L., & Ross, J., Jr (1994). ANG II receptor blockade prevents ventricular hypertrophy and ANF gene expression with pressure overload in mice. *The American journal of physiology, 266(6 Pt 2),* H2468–H2475.

Sadoshima, J., & Izumo, S. (1993). Signal transduction pathways of angiotensin II--induced c-fos gene expression in cardiac myocytes in vitro. Roles of phospholipid-derived second messengers. *Journal Of Circulation Research,* 73(3), 424–438.

Schunkert, H., Sadoshima, J., Cornelius, T., Kagaya, Y., Weinberg, E. O., Izumo, S., Riegger, G., & Lorell, B. H. (1995). Angiotensin II-induced growth responses in isolated adult rat hearts. Evidence for load-independent induction of cardiac

protein synthesis by angiotensin II. *Journal of Circulation research,* 76(3), 489–497.

Segar, J. L., Dalshaug, G. B., Bedell, K. A., Smith, O. M., & Scholz, T. D. (2001). Angiotensin II in cardiac pressure-overload hypertrophy in fetal sheep. American journal of physiology. *Regulatory, integrative and comparative physiology,* 281(6), R2037–R2047.

Simeone, R. M., Devine, O. J., Marcinkevage, J. A., Gilboa, S. M., Razzaghi, H., Bardenheier, B. H., Sharma, A. J., & Honein, M. A. (2015). Diabetes and congenital heart defects: a systematic review, meta-analysis, and modeling project. *American journal of preventive medicine,* 48(2), 195–204.

Somaratne, J. B., Whalley, G. A., Poppe, K. K., ter Bals, M. M., Wadams, G., Pearl, A., Bagg, W., & Doughty, R. N. (2011). Screening for left ventricular hypertrophy in patients with type 2 diabetes mellitus in the community. *Journal of Cardiovascular diabetology,* 10, 29.

Sundgren, N. C., Giraud, G. D., Stork, P. J., Maylie, J. G., & Thornburg, K. L. (2003). Angiotensin II stimulates hyperplasia but not hypertrophy in immature ovine cardiomyocytes. *The Journal of physiology,* 548(Pt 3), 881–891.

Timpka, S., Macdonald-Wallis, C., Hughes, A. D., Chaturvedi, N., Franks, P. W., Lawlor, D. A., & Fraser, A. (2016). Hypertensive Disorders of Pregnancy and Offspring Cardiac Structure and Function in Adolescence. *Journal of the American Heart Association,* 5(11), e003906.

Valensise, H., Novelli, G. P., Vasapollo, B., Di Ruzza, G., Romanini, M. E., Marchei, M., Larciprete, G., Manfellotto, D., Romanini, C., & Galante, A. (2001). Maternal diastolic dysfunction and left ventricular geometry in gestational hypertension. *Journal of Hypertension (Dallas, Tex.: 1979),* 37(5), 1209–1215.

Visentin, S., Grumolato, F., Nardelli, G. B., Di Camillo, B., Grisan, E., & Cosmi, E. (2014). Early origins of adult disease: low birth weight and vascular remodeling. *Journal of Atherosclerosis,* 237(2), 391–399.

Wikström, A. K., Haglund, B., Olovsson, M., & Lindeberg, S. N. (2005). The risk of maternal ischaemic heart disease after gestational hypertensive disease. *BJOG : an international journal of obstetrics and gynaecology,* 112(11), 1486–1491.

Yang, X., Dormann, D., Münsterberg, A. E., & Weijer, C. J. (2002). Cell movement patterns during gastrulation in the chick are controlled by positive and negative chemotaxis mediated by FGF4 and FGF8. *Developmental cell,* 3(3), 425–437.

Yogev, Y., Chen, R., Ben-Haroush, A., Hod, M., & Bar, J. (2010). Maternal overweight and pregnancy outcome in women with Type-1 diabetes mellitus and different degrees of nephropathy. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians,* 23(9), 999–1003.

Zaffran, S., Kelly, R. G., Meilhac, S. M., Buckingham, M. E., & Brown, N. A. (2004). Right ventricular myocardium derives from the anterior heart field. *Circulation research,* 95(3), 261–268.

Zangen, S. W., Yaffe, P., Shechtman, S., Zangen, D. H., & Ornoy, A. (2002). The role of reactive oxygen species in diabetes-induced anomalies in embryos of Cohen diabetic rats. *International journal of experimental diabetes research,* 3(4), 247–255.

ARABIC SUMMARY

تضخم القلب: اضطراب الحمل الجنيني

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يعد تضخم القلب عاملاً خطيرًا رئيسيًا لأمراض القلب المختلفة، وهو أحد العيوب الخلقية الجنينية والسبب الرئيسي لوفيات الأطفال عالميا. يتميز هذا التشوه بزيادة سمك عضلة القلب، مما يؤدي الى اتساع في حجم غرفه، حتى يستطيع القلب ضخ الدم إلى الأنسجة والأعضاء حول الجسم.

تعد النساء الحوامل اللاتي لديهن تاريخ عائلي أو اللاتي أصبن بداء السكري قبل الحمل أو تسمم الحمل أو ارتفاع ضغط الدم هن أكثرالنساء عرضة لخطر حمل جنين أو إنجاب طفل مصاب بتضخم قلبي. تتفاوت أعراض المرض بين أعراض بسيطة إلى شديدة، وقد تشمل الأعراض ألم في الصدر، وكذلك ضيق التنفس. أما بالنسبة لتشخيص المرض فيتم على أساس التاريخ الطبي، والفحص البدني ونتائج فحص مخطط صدى القلب. تتمثل طرق الوقاية والعلاج من هذا الخلل من خلال عدة طرق أهمها تعديل نمط الحياة وتجنب السمنة واستخدام الأدوية وأحياناً اللجوء الى الجراحة إذا تطلب الأمر. الهدف من البحث الحالي هو استعراض المسببات والتشخيص وأسباب هذا التشوه الخلقي وطرق الوقاية والعلاج في الأجنة أو بعد الولادة.

الكلمات المفتاحية: تضخم القلب، أمراض القلب الخلقية، الحمل، الجنين.