Glycodeline-A , PlGF Together with βhCG as Prognostic Markers in First Trimester Pregnancy Loss for Iraqi Women

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Abstract

Objective: estimate the scale of Glycodeline-A,PlGF, together with βhCG in first trimester pregnancy loss in Iraqi women .

Methods: A subject:patients and control study, begining in April 2019 and finish the work at March 2020, study include 85 women,45 of them as healthy control which haven't any complication at the first trimester stsrting from the first day of LMP , 40 of them as patients which have abortion at the same time,tests included evaluate the scale of βhCG,Glycodeline-A,PlGF By ELISA method.

Results: scale of βhCG are significantly higher in healthy controls than in patients , while scale of Glycodeline-A , PlGF was significantly lower in healthy control than in patients,and there is significant correlation among each of ges.age with βhCG and PlGF $P < 0.05$.

Conclusion: This study suggest that the significant role of Glycodeline-A,PlGF in etiologies of first trimester pregnancy failed and some of them was related to βhCG in this time and the age of patients wasn't effect on all of these parameters.

Keywords: *βhCG, Glycodeline-A,PlGF*

Introduction

The most important basic cell differentiation of fetal occur during the first three months of pregnancy , so any complication done to the fetus during this period is leading to result represent miscarriage or serious complications According to the first three trimesters of pregnancy[1] , fallopian tube delivered the egg which is fertilized and attaches to the inside of the woman,s uterus , where it begins to configure the embryo and placenta , mudding of gestational age can be occured[2] , women think of pregnancy as a a nine months lasting , this is true when that the women lasting nine months , while the measured of this is begin with the first day of the last period for them and about three to four weeks before they are become pregnant , pregnancy usually lasts about fourty weeks for pregnancy age this period is about ten months[3], Miscarriage defined as a failed or loss of pregnancy before twenty weeks from the first day of last period and it is known as pregnancy loss and spontaneous abortion[4] , it is the death naturally of fetus before it is able to life independently , the first trimester of pregnancy starts from the first day of last menstrual period and end in the twelve weeks of pregnancy , miscarriage is common at this period[5], Blood investigations and genetic study , must be doing if a planning to manage the woman which has more than two losses of her carry or more in a situation identified as recurrent miscarriage , many procedures may be used to detect the reason of repeated miscarriage include ultrasound of pelvic , hysterosalpingogram which is include x-ray of the uterus tubes and uterus itself , and hysteroscopy which is include views interior of the uterus,[6] The first trimester pregnancy loss is common , depending on the (ACOG), it happens in ten percent of confirmed pregnancies , the cause of a miscarriage sometimes will remain unknown,

however , the (ACOG) decide that about fifty percent of miscarriages are chromosome issues abnormality , the miscarriage risk definitely increases with age[7] , according to the (ACOG) , the miscarriage risk is twenty percent at age thirty five , and increased to fourty percent at age fourty and increased further to eighty percent at age fourty five [8], the main type of miscarriages is unprompted abortions which characterized by unprotected , they are unexpected effects which are differ from recur , high percent of first and second trimester pregnancy loss are due to chromosomal abnormalities , and the other are include many problems affect these carries like infected disease[9] , uterus and cervix problems , smoking , toxins exposure , harmful substance abuse , high level of glucose , problems of thyroxin hormones secertion , harmful disease of autoimmune , advanced age of women which carry are more miscarry than lower subjects[10] , sometimes physical trauma accident may cause failed these carries , at common knowledge , the main cause for these results of disadvantage carry is obscure, By tissue of trophoplast created of βhCG[11], component of fetus existing at early time of pregnancy and represent a placenta portion , determining of this substances can be helpe in differentiate a normal or abnormal carry , and can be using in the prognose of failed carry , an advantage for determining of hCG in a various tumors for womb malignancies,while Glycodelin - A produced from decidual glandular epithelium and endometrial glands , get its effect and supply in the early pregnancy[12] , GdA contribute in primary placental grow by its involving supply on trophoplast and immune units, PlGF is a homodimeric growth factor that contributes with VEGF , it can form heterodimers with some types of VEGF and inhibit the angiogenic effect of VEGF on VEGF R2 , blood circulating PlGF levels increase through pregnancy , reaching a peak in second trimester of gestation , this increase is weak in preeclampsia[13] , PlGF stimulates monocyte effect and migration as well as lead to produced of inflammatory cytokines and VEGF, these activities facilitate bone fracture , wound , and cardiac repair , but also contribute to inflammation in active sickle cell disease and atherosclerosis , PlGF can also decrease TIMP3 expression in the spleen , leading to triggering of immune in hypertension[14] .

Aim of the study: to estimate the scale of Glycodeline-A , PlGF together with βhCG as prognostic markers of first trimester pregnancy loss in Iraqi women.

Method

Study design: The present project was perfected at the department of Biochemistry , Medicine College , Baghdad University , at Hospital of Baghdad Teaching through the time from April 19 to March 2020 , it included 85 pregnant woman identified the first day of LMP who are confirmed positive pregnancy test in blood , and established to have had pregnancy by Consultant Gynaecologist and matching age 21 – 35 year and same time 8 – 12 week of pregnancy and encountered during their attendance the Gynaecology consultation clinic at Baghdad Teaching hospital , encountered these women until the end of week 12 of pregnancy , 40 of them who have pregnancy loss at the prognosis period are patients and the other 45 healty control who completed the same period without problems , a written consent was applied by each patient and an ethical approval had been suitable the researcg based of the Medicine College , Baghdad University and the link with Ministry of Health and enviroment.

Data Setting: Eight to ten milliliters (mls) of blood from subjects are draw out and transferred into plain tube , allows for half hour to sure that is clotting , after this , the specimen must be centrifuged to separated the needed serum at 2500 rpm for limited time roughly ten minuted and stored at freezing degree about – 20 Co up to beginning of the assay the project biochemical markers : Beta HCG , Glycodeline-A , sFlt-1 , PlGF By ELISA method .

Inference by statistics: Inference by statistics is a method that analysis of details by using SPSS , this information were putting as simple measures of variants (mean , standard deviation and others) , qualitative detailes which are significant statistically were using student-t-test for compare between two independent means or ANOVA test for compare between different qualitative detailes on , the statistical significance is equal or less than 0.05 , the coefficient of correlation value r : is a kind of coefficient correlation clarify the connection between two different factors that are calculated on the same period , r may be positive as direct correlation or negative as inverse correlation.

Results

Explane by table scales of of various markers and

their correlations according to the study assessment .

Table 1: Results and their obtained correlations for all markers in this study

Group Statistics

	VAR00013	N	Mean	Std. Deviation	Std. Error Mean
Age cAge	1.00	40	27.1250	4.18292	.66138
	2.00	45	27.2444	4.11293	.61312
GestAge c GestAge	1.00	40	9.6000	1.29694	.20506
	2.00	45	9.5333	1.09959	.16392
BetaHCG cBetaHCG	1.00	40	1024.7740	459.39406	72.63658
	2.00	45	2309.9409	3007.11697	448.27453
GlycodeinA cGlycodlinA	1.00	40	70.9447	56.87327	8.99245
	2.00	45	193.7416	200.56648	29.89868
PIGF CPIGF	1.00	40	141.4350	284.10843	44.92149
	2.00	45	340.2947	387.01779	57.69321

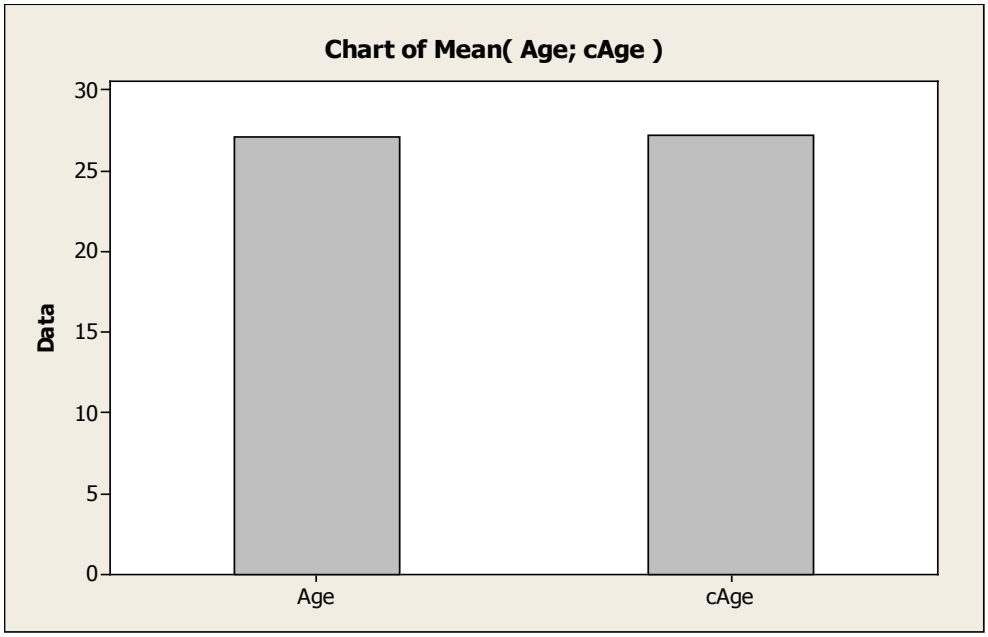

Figure1:Chart of mean (Age , cAge).

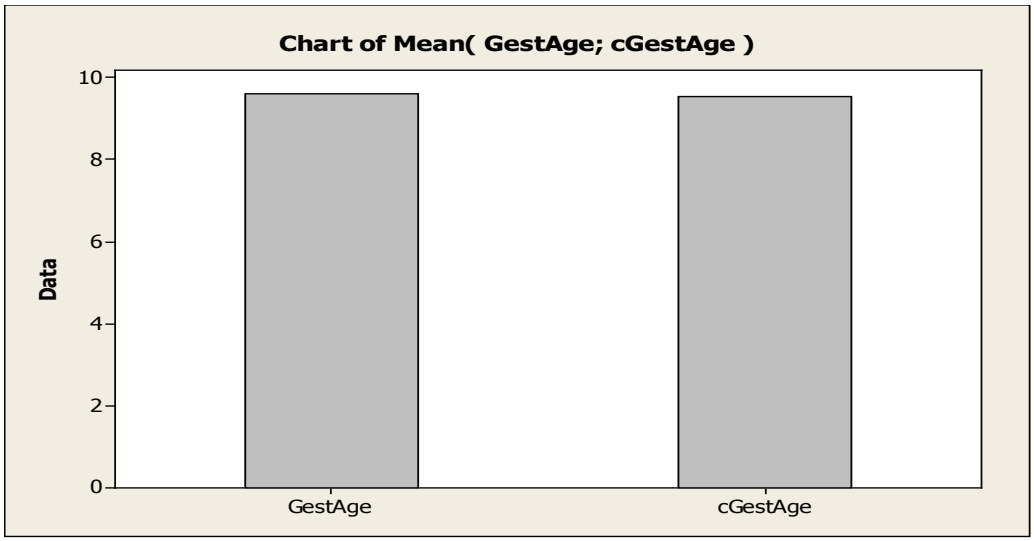

Figure2:Chart of mean (Gest. age , cGestational age)

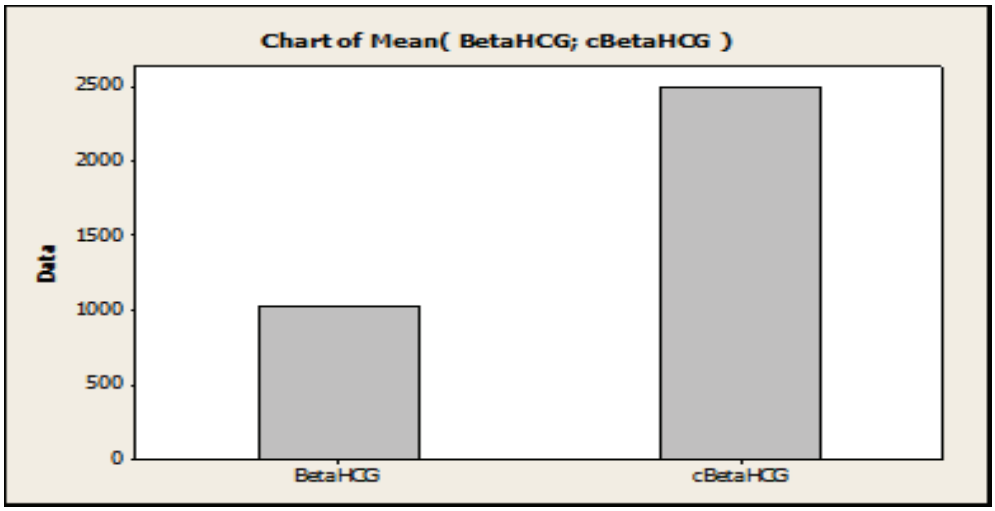

Figure3:Chart of (βhCG, cβhCG)

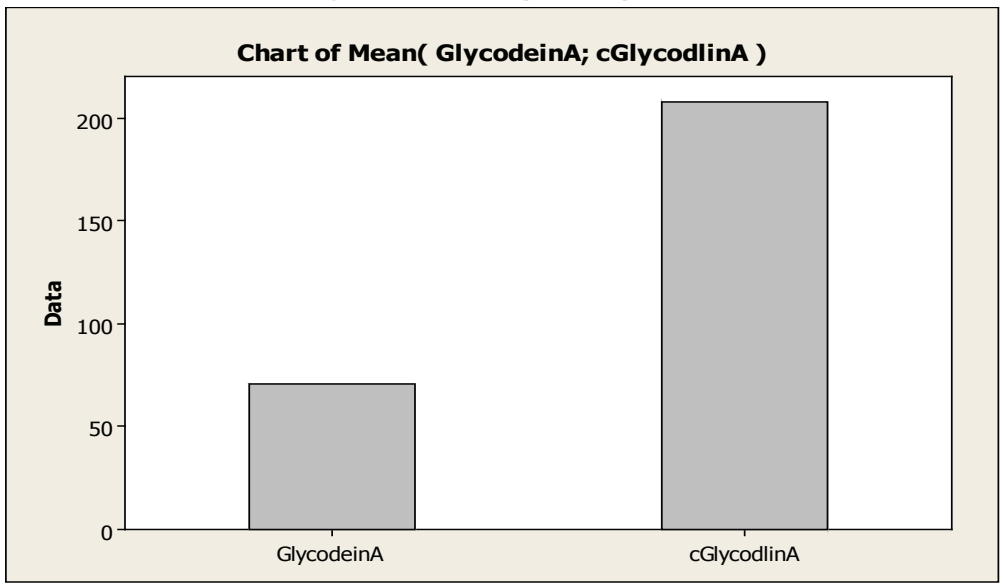

Figure4:Chart of (Glycodelin-A , cGlycodeline-A)

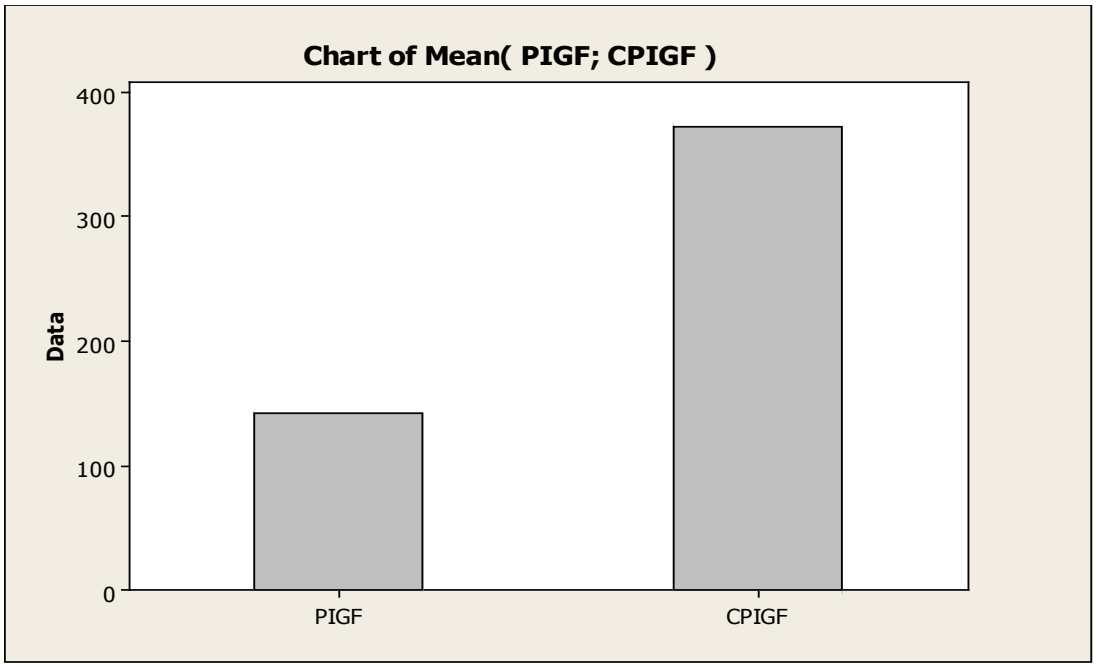

Figure6:Chart of (PlGF , cPlGF)

Discussion

Serum level of βhCG in healthy control group (mean ± SD 2309.940 ±3007.116) in patients which have abortion (1024.774 ±4 59.394) which show significant correlation : P value 0.05 , that mean the level of this marker in patients was lower than in healthy control , The present study shows that the serum level of glycodelin-A in healthy control group (mean ± SD 193.741 ± 200.566) , in patients which have abortion (70.944 ± 56.873) which show significant correlation : P value 0.01 , that mean the level of this marker in patients was lower than in healthy control , The present study shows that the serum level of PlGF in healthy control group (mean ± SD 340.294 ± 387.017) , in patients which have abortion (141.453 ± 284.108) which show significant correlation : P value 0.05 , that mean the level of this marker in patients was lower than in healthy control , most of previous projects have found that the chromosomal agents are effective factor in carry loss[15] , old studies have demonstrated that the normal carry depends on normal immune system which is consist of immune defence , immune response , cytokines[15] , the immune effect is important factor in first carry failed , the immune units that establish at the mediater of placenta and the uterus were stay overlap layer of arrangment by immunity system of mother , this process may help of placental growth but some times reduce the placental aggress the embryo , in the time of implantation natural killer units go to the uterus and help the stimulation secrete of cytokines that inhibit the trophoblast aggress[16].

Conclusion

levels of all markers according to the result which obtained from the assessment of them are clarify the relation between patients which have abortion in the first trimester and healty control , these results suggest for βhCG: level of this marker in patients was lower than in healthy control,and for Glycodelin-A: level of this marker in patients was lower than in healthy control,and for PlGF: level of this marker in patients was lower than in healthy control .

Ethical Approval: Describe written consent was applied by each patient and an ethical approval had been suitable the researcg based of the Biochemistry Department,Medicine College, Baghdad University and the link with Iraqi Ministry of Health .

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Ethical Clearance: Not Required

References

1. Kolte AM , Olsen LR , Mikkelsen EM , Christiansen OB , Nielsen HS, Depression and emotional stress is highly prevalent among women with recurrent pregnancy loss. 2019 ; 30(4) :777–782 ,
2. Brezina PR , Kutteh WH, Clinical applications of preimplantation genetic testing . 2017 ; 350:g 7611.
3. Ikuma S , Sato T , Sugiura-Ogasawara M , Nagayoshi M , Tanaka A , Takeda S , Preimplantation genetic diagnosis and natural conception : a comparison of live birth rates in patients with recurrent pregnancy loss associated with translocation . 2019;10(6):e0129958.
4. Kutteh WH , Bernardi LA , strategies for the management of recurrent pregnancy loss . 2019 ; 125(5) : 1258–1267.
5. Hazard FK , Lathi RB , Early pregnancy loss . 2015 ; 114(6) : 907–921.
6. Kling C , Magez J , Hedderich J , von Otte S , Kabelitz D, Two-year outcome after recurrent first trimester miscarriages: prognostic value of the past obstetric history. 2016 ; 293(5) : 1113–1123 ,
7. Pereza N , Ostojić S , Kapović M , Peterlin B, Systematic review and meta-analysis of genetic association studies in idiopathic recurrent spontaneous abortion. 2017; 107(1): 150–159.e2.
8. Shi X , Xie X , Jia Y , Li S, Maternal genetic polymorphisms and unexplained recurrent miscarriage : a systematic review and meta-analysis . 2017 ; 91 (2) : 265–284.
9. Zhang M , Xu J , Bao X , et al., Association between genetic polymorphisms in interleukin genes and recurrent pregnancy loss – a systematic review and meta-analysis . *PLoS ONE* . 2017 ; 12(1) : e0169891.
10. Meuleman T , Lashley LE , Dekkers OM , van Lith JM , Claas FH , *Hum Immunol*, HLA associations and HLA sharing in recurrent miscarriage : a systematic review and meta-analysis . 2019 ; 76(5) : 362–373.
11. Mekinian A , Cohen J , Alijotas-Reig J , et al. , *Am J Reprod Immunol*. Unexplained recurrent miscarriage . 2016 ; 76(1) : 8–28.
12. Schleussner E , Kamin G , Seliger G , et al., Low-molecular-weight heparin for women with unexplained recurrent pregnancy loss . 2015 ; 162(9) : 601–609 .
13. Pasquier E , de Saint Martin L , Bohec C , et al., Enoxaparin for prevention of unexplained recurrent miscarriage : a multicenter randomized double-blind placebo-controlled trial . 2018 ; 125(14) : 2200–2205 , .
14. Robertson SA , Jin M , Yu D , et al. Corticosteroid therapy in assisted reproduction – immune suppression . 2019 ; 31(10) :2164–2173 ,.
15. Kemp MW , Newnham JP , Challis JG , Jobe AH , Stock SJ, The clinical use of corticosteroids in pregnancy . 2018 ; 22(2) : 240–259.
16. Christiansen OB , Larsen EC , Egerup P , Lunoee L , Egestad L , Nielsen HS , Intravenous immunoglobulin treatment for secondary recurrent miscarriage. 2019 ; 122(4) : 500–508.