Pregnancy Hypertension 17 (2019) 49–53

Contents lists available at ScienceDirect

Pregnancy Hypertension

journal homepage: www.elsevier.com/locate/preghy

Association of MicroRNA-210 and MicroRNA-155 with severity of preeclampsia

Hanan Mohamed Gabr Youssef*,[1], Elham Sayed Marei[1]

Health Radiation Research Department, National Center for Radiation Research and Technology, Egyptian Atomic Energy Authority, Cairo, Egypt

ARTICLE INFO

Keywords:
MicroRNA-210
MicroRNA-155
Mild Preeclampsia
Severe Preeclampsia

ABSTRACT

Backgrounds and objectives: Preeclampsia (PE) is one of the leading causes of maternal and neonatal morbidity and mortality. Preeclampsia is associated with aberrant expression of several MicroRNAs which function as gene regulators. The present study aims to determine the expression of MicroRNA-210 and MicroRNA-155 in Preeclampsia, and to detect the association of MicroRNA-210 and MicroRNA-155 levels with the severity of Preeclampsia.

Methods: The study was carried out on thirty PE pregnant women as the Preeclampsia group compared to twenty healthy pregnant women who served as the control group. The patients were chosen at labor wards from Ain Shams Maternity Hospital during the period from June to December 2016. Preeclampsia group was then subdivided into mild Preeclampsia and severe Preeclampsia subgroups according to the levels of arterial blood pressure with the presence of thrombocytopenia, impairment in liver function, progressive renal insufficiency, pulmonary edema and cerebral or visual disturbance. MicroRNA-210 and MicroRNA-155 were estimated by a quantitative real time polymerase chain reaction (qRT-PCR).

Results of this study showed that the levels of MicroRNA-210 and MicroRNA-155 detected in the Preeclampsia group are significantly higher than in the control group. Although MicroRNA-210 levels showed high significant increase in severe PE compared to mild PE cases, there were no significant differences in MicroRNA-155 levels between the two PE subgroups detected.

Conclusions: MicroRNA-210 may be the noncoding RNA at the molecular level in which the increase in its level accompanies the progression of PE; and is closely associated with the severity of Preeclampsia.

1. Introduction

Preeclampsia is a pregnancy associated multisystem disorder due to endothelial dysfunction and end organ ischemia, which affects 3–8% of pregnancies worldwide [1] and causes maternal and perinatal morbidity and mortality throughout the world. In a recent study case, the fatality rate of Preeclampsia was 2.26% and eclampsia was 4.1% [2]. PE, whether mild or severe, can develop to eclampsia, maternal multiorgan damage and death [3].The Preeclampsia is now defined as hypertension developing after 20 weeks' gestation with one or more of the following: proteinuria, maternal organ dysfunction (including renal, hepatic, hematological, or neurological complications), or fetal growth restriction [4]. According to this definition, no proteinuria is required to diagnose PE. Preeclampsia is categorized as severe if systolic BP is 160 mmHg or higher, diastolic BP of 110 mmHg or higher, with one or more of these clinical findings: thrombocytopenia less than 100.000/microliter, impaired liver function (elevated liver enzymes or severe right upper quadrant or epigastric pain), progressive renal insufficiency (creatinine more than 1.1), pulmonary edema and cerebral or visual disturbance. If such clinical findings are associated with BP 140/90, it is also considered severe Preeclampsia [5].

Studies on MicroRNAs demonstrated the existence of placental MicroRNAs in maternal plasma, which modulate gene expression in the maternal compartment [6]. MicroRNAs belong to short non-coding molecules that regulate gene expression at post-transcriptional level [7]. A thirty percent of human genes are regulated by MicroRNAs' transcriptions, which have a key role in several cellular processes; including cell growth, proliferation, differentiation and apoptosis [8].

Certain deregulated MicroRNAs recorded in PE are specific for the placenta as well as the liver, the brain, the immune system and the kidney. Therefore, PE is considered a multisystem disorder because any deregulation of these MicroRNAs affects the normal function of target

* Corresponding author.
E-mail address: hanangabr62@gmail.com (H.M.G. Youssef).
[1] National Center for Radiation Research and Technology, Egyptian Atomic Energy Authority, Ahmed El-Zomor Street, Nasr City, Cairo 11371, Egypt.

https://doi.org/10.1016/j.preghy.2019.05.010
Received 2 October 2018; Received in revised form 13 April 2019; Accepted 8 May 2019
Available online 10 May 2019

genes in the placenta as well as in those systems [9].

In Preeclampsia, the events that occur normally in placental development will occur abnormally, due to the aberrant expression of MicroRNAs, resulting in impaired cytotrophoblast differentiation and apoptosis, incomplete spiral artery invasion and decreased blood flow to and from the placenta. Trophoblast necrosis triggers a systemic immunological response and oxidative stress in the placenta [10].

The MicroRNA-210 is considered as hypoxia-associated, that is up-regulated by hypoxia [11], and is also considered a potential serum biomarker for PE [12]. MicroRNA-210 is associated with pathogenesis of PE; up-regulation is correlated with the inhibition of migration and the invasive capability of trophoblasts, and is linked to induction of the activity of several intracellular transcription factors [13].The aberrant expression of MicroRNA-210 may contribute to the occurrence of PE by regulating the trophoblast cell invasion via targeting potassium channel modulatory factor-1 mediated signaling in the human placenta [14].

Researchers demonstrated that overexpression of MicroRNA-155 contributed to Preeclampsia by down-regulating cysteine-rich angiogenic inducer 61 (CYR61) which is an early angiogenic regulating factor during pregnancy, and reducing the stability of (CYR61) mRNA, which leads to local ischemia and oxidative stress [15].

The present study was carried out to determine the relative expression of MicroRNA-210 and MicroRNA-155 in Preeclampsia (mild and severe) compared to the control group, and to find the possible association of MicroRNA-210 and MicroRNA-155 with the severity of Preeclampsia.

1.1. Subjects and methods

A total number of 50 pregnant women, who attended Ain Shams Maternity Hospital from June to December 2016, at labor wards, were enrolled in this study. Thirty pregnant patients who were previously diagnosed as preeclamptic patients were chosen as Preeclampsia group. The (30) PE patients were further classified into mild (n = 12) and severe Preeclampsia (n = 18) subgroups in accordance with the classification of [The International Society for the Study of Hypertension in Pregnancy, ISSHP], which classified PE as: mild PE, with a maternal systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg, with significant proteinuria (≥1+ by dipstick) at 20 to 34 weeks of gestation; and the [ISSHP] agreed to define "severe Preeclampsia" by blood pressure values > 160 mmHg systolic or 110 mmHg diastolic and the amount of proteinuria is considered not useful to define the severity. If thrombocytopenia increase in liver or kidney functions, persistent epigastric pain, pulmonary edema, cerebral or visual disturbances are present, the patients are categorized as severe PE subgroup even with mild hypertension [5]. The control group included (20) healthy pregnant women without any pregnancy complications who came for delivery between 38 and 40 weeks gestation. Exclusion criteria included pregnant women with no pregnancy complications or systemic diseases. Informed consents were completed by all subjects. The procedures performed involving human participants were according to Helsinki declaration. The study was approved by the Ethical committee of National Center for Radiation Research and Technology.

All participants were subjected to clinical examinations with measurements of the blood pressure. Systolic and diastolic blood pressures were determined then, the mean arterial blood pressure for each subject was calculated according to the following equation: $MABP = \frac{(2 \times \text{diastolic BP}) + \text{systolic BP}}{3}$. The laboratory investigations (hemoglobin, platelets, urine albumin, serum albumin, ALT, AST, Creatinine, urea, and INR) were performed for all subjects.

Blood samples were collected on admission for labor; serum was separated and collected in aliquots. The serum aliquots were frozen at −80 °C.

1.2. RNA extraction

Total RNA was extracted from 100 µL of serum using the MirVana PARIS kit (Ambion, Warrington, UK) according to the manufacturer's instructions. The concentration and purity of RNA were determined using NanoDrop® ND-1000. The RNA concentration and purity were confirmed by the spectrophotometric ratio using absorbance measurements at wavelengths of (260 and 280 nm) on a Beckman DU 640UV spectrophotometer (Beckman, Fullerton, CA). The (260/280) absorbance ratio of isolated RNA was 1.8–2.0, demonstrating that the RNA fraction was pure and could be used for analysis.

1.3. Quantitative real-time PCR

RNA (5 µg) per 20-µL reaction to generate cDNA using Gene-specific primers from the TaqMan MicroRNA was used. Assays and reagents from the TaqMan MicroRNA, Reverse Transcription kit (Applied Biosystems, Foster City, CA, USA), real-time PCR were carried out using an Invitrogen kit. Primers sequence for MiR-210 and MiR-U6 were: forward 5′CUGUGCGUGUGACAGCGGCUGA-3′,5′ GCTTCGGCAGCACA TATACTAAAAT-3′; and reverse: 5′ AGCCGCUGUCACACGCACA GUU-3′,5′CGCTTCACGAATTTGCGTGTCAT3′.

For miR-155 detection, sequences of forward and reverse primers were as follows: 5′-CTGTTAATGCTAATCGTGATAG-3′ and 5′-GCAGGGTCCGA GGT-3′ in Step One Plus (Applied Biosystem, USA) device. MicroRNA expressions were normalized to small RNA U6, with the similar efficiency of MicroRNAs. Data of quantitative RT-PCR was demonstrated by nominal CT value (normalized toU6), and fold changes were calculated by ΔΔCt. The ΔΔCt calculated as (ΔΔCt = ΔC samples − ΔCt control) to qualify the expression rate of MiR-210 and MiR-155 reference.

Statistical analysis was performed using SPSS version 20 statistical software (SPSS, Inc., Chicago, IL) and a *P*-value of < 0.05 is considered statistically significant. All the results are defined as mean ± standard deviation. The independent sample-*t* test was applied to compare the MicroRNAs expression levels, and the other measured parameters between PE group and control group. One-way ANOVA test was applied for comparison between mild PE, severe PE and control groups.

Table 1
The clinical data and laboratory investigations of Preeclampsia group compared to the control group.

Parameters	Preeclampsia (n = 30) Mean ± SD	Control (n = 20) Mean ± SD	P-values
Age (years)	31.77 ± 3.159	29.75 ± 4.241	0.078
Parity	2.10 ± 0 0.960	1.80 ± 0.768	0.227
Systolic BP (mmHg)	162.00 ± 19.19	114.5 ± 6.66	0.0001**
Diastolic BP (mmHg)	105.0 ± 12.24	69.5 ± 9.30	0.0001**
Mean blood pressure	123.95 ± 14.12	84.44 ± 8.08	0.0001**
Gestational age (weeks)	36.1 ± 3.47	38.6 ± 0.94	0.01*
Fetal birth weight (gm)	2659.33 ± 571.16	3480.00 ± 308.82	0.0001**
Urine albumin (gm/dl)	2.1 ± 1.06	0	0.0001**
Hemoglobin (gm/dl)	11.65 ± 1.03	11.21 ± 0.73	0.085
ALT (U/L)	38.00 ± 21.85	16.40 ± 2.39	0.001**
AST (U/L)	40.23 ± 14.40	18.30 ± 2.79	0.001**
Urea (mg/dl)	26.30 ± 13.01	21.40 ± 3.21	0.071
Creatinine (mg/dl)	0.941 ± 0.603	0.795 ± 0.178	0.132
Platelet count ($\times 10^3$/µl)	167.30 ± 33.18	218.3 ± 39.98	0.0001**
INR	0.998 ± 0.014	0.994 ± 0.015	0.359
Serum albumin (gm/dl)	2.98 ± 0.49	3.55 ± 0.068	0.01*
MicroRNA210 (relative expression)	5.84 ± 3.38	1.02 ± 0.06	0.0001**
MicroRNA-155 (relative expression)	2.92 ± 0.48	1.40 ± 0.35	0.0001**
No. of Cesarean Section Delivery (%)	16 (53.33%)	7 (35%)	0.001**

Table 2
Correlation between MicroRNA-210 and different clinical and laboratory investigated parameters in Preeclampsia group (n = 30).

Pearson correlation	GA	Parity	Systolic BP	Diastolic BP	Mean ABP	ALT	AST	Creatinine	Urea	Urine albumin	Serum albumin	Fetal weight
MicroRNA-210 r	−0.365	−0.096	0.858	0.841	0.875	0.029	0.357	0.505	0.426	0.343	0.109	−0.418
p-values	0.047	0.614	0.000	0.000	0.000	0.879	0.053	0.004	0.019	0.064	0.565	0.02
Sig. (2-tailed)	**Sig.**	**NS**	**HS**	**HS**	**HS**	**NS**	**NS**	**HS**	**Sig.**	**NS**	**NS**	**Sig.**

Table 3
Correlation between MicroRNA-210 with different clinical and laboratory investigated parameters in all subjects (n = 50).

Pearson correlation	GA	Parity	Systolic BP	Diastolic BP	Mean A BP	ALT	AST	Creatinine	Urea	Urine albumin	Serum albumin	Fetal weight
MicroRNA-210r r	−0.521	0.054	0.898	0.854	0.882	0.379	0.656	0.458	0.455	0.687	−0.0333	−0.655
p-values	0.000	0.711	0.000	0.000	0.000	0.007	0.000	0.001	0.001	0.000	0.018	0.000
Sig. (2-tailed)	**HS**	**NS**	**HS**	**HS**	**HS**	**HS**	**HS**	**HS**	**HS**	**HS**	**Sig.**	**HS**

Table 4
Correlation between MicroRNA-155 and different clinical and laboratory investigated parameters in Preeclampsia group (n = 30).

Pearson correlation	GA	Parity	Systolic BP	Diastolic BP	Mean ABP	ALT	AST	Creatinine	Urea	Urine albumin	Serum albumin	Fetal weight
MicroRNA-155r r	0.083	0.032	−0.178	−0.230	−0.213	−0.136	0.043	−0.124	−0.143	−0.078	0.118	0.177
p-values	0.661	0.868	0.346	0.222	0.257	0.474	0.823	0.513	0.452	0.686	0.536	0.350
Sig. (2-tailed)	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**

2. Results

The data in Table 1 reveals that there are no significant differences in maternal age, parity, hemoglobin, urea, creatinine and INR between PE and control groups. However, there are significant differences in gestational age at delivery and serum albumin between PE and control groups. There are also high significant differences in systolic, diastolic and mean arterial blood pressure, fetal birth weight, urine albumin, ALT and AST, MicroRNA-210 and MicroRNA-155 between PE and control groups. The Cesarean Section deliveries are significantly higher in PE group than the control group.

Table 2 shows no significant correlation between MicroRNA-210 and parity, ALT, AST, urine albumin, serum albumin and INR, but inverse significant correlation between MicroRNA-210 with gestational age and fetal birth weight in the PE group. There are high significant correlations between MicroRNA-210 with systolic, diastolic, mean arterial blood pressure and creatinine.

Table 3 shows the significant inverse correlation between MicroRNA-210 with gestational age, fetal birth weight and serum albumin in all subjects and also high direct significant correlation with systolic, diastolic, mean blood pressure, ALT, AST, creatinine, urea and urine albumin.

Table 4 demonstrates that in Preeclampsia group there are non-significant correlations between MicroRNA-155 with GA, parity, systolic, diastolic, mean ABP, ALT, AST, creatinine, urea, urine, serum albumin and fetal birth weight.

Table 5 shows the high significant differences in mean ABP, gestational age, Fetal birth weight, MicroRNA-210 and MicroRNA-155 between the mild, severe PE and control groups.

Table 6 clarifies the significant difference in systolic, diastolic, mean ABP, urine albumin, creatinine, gestational age, fetal birth weight, and MicroRNA-210; the non significant differences in urea, ALT, AST, serum albumin and MicroRNA-155 between mild and

Table 6
Comparison between mild PE subgroup (n = 12) and severe PE subgroup (n = 18) in clinical and biochemical data.

Parameter	Group	N	Mean	Std. Deviation	p-value
Systolic BP	mild PE	12	145.00	5.22	0.000**
	severe PE	18	173.33	16.45	
Diastolic BP	mPE	12	92.50	4.52	0.000**
	sPE	18	113.33	7.67	
Mean BP	mPE	12	109.95	4.26	0.000**
	sPE	18	133.28	7.67	
Urine Albumin	mPE	12	1.50	0.904	0.008**
	sPE	18	2.50	0.985	
Creatinine	mPE	12	0.642	0.068	0.024*
	sPE	18	1.14	0.716	
Urea	mPE	12	22.25	1.54	0.168
	sPE	18	29.00	16.36	
ALT	mPE	12	33.00	14.60	0.315
	sPE	18	41.33	25.44	
AST	mPE	12	34.33	19.43	0.066
	sPE	18	44.17	8.28	
Serum Albumin	mPE	12	2.97	0.513	0.914
	sPE	18	2.99	0.491	
GA	mPE	12	37.75	1.35	0.014*
	sPE	18	35.00	4.02	
Fetal weight	mPE	12	2975.0	169.8	0.000**
	sPE	18	2448.8	548.5	
Micro RNA-210	mPE	12	3.21	1.84	0.000**
	sPE	18	7.63	2.93	
MicroRNA-155	mPE	12	3.00	0.51	0.466
	sPE	18	2.87	0.48	

Table 5
Comparison between mild PE, severe PE and control groups in mean ABP, gestational age, fetal birth weight, MicroRNA-210 and MicroRNA-155 by using one way-ANOVA.

Parameters	Mild PE (n = 12)	Severe PE (n = 18)	Control (n = 20)	*P-value*
Mean ABP	109.95 ± 4.26	133.28 ± 7.67	84.44 ± 8.08	0.0001
Gestational age	37.75 ± 1.35	35.00 ± 4.02	38.6 ± 0.94	0.001
Fetal birthweight	2975.0 ± 169.8	2448.8 ± 548.5	3480.0 ± 308.8	0.003
MicroRNA-210	3.21 ± 1.84	7.63 ± 2.93	1.02 ± 0.06	0.0001
MicroRNA-155	3.00 ± 0.51	2.87 ± 0.48	1.40 ± 0.35	0.01

severe Preeclampsia subgroups.

3. Discussion

The exact pathogenesis of PE remained unclear. The identification of MicroRNAs which were up-regulated or down-regulated in PE suggested their utility as biomarkers. It was not established whether MiRNA-210 and MiRNA-155 contributed to the pathological changes of Preeclampsia or were just the consequence at late gestation. There were challenges in addressing the discrepancy between the pathophysiological changes that were initiated before 20 weeks gestation and the clinical symptoms that manifested after 20 weeks gestation [16]. Circulating MiRNAs in pregnant women were suggested to be mainly coming from the placenta [6,17].

In the present study, the results demonstrated that the PE group had high significant increases in relative expressions of MicroRNA-210 with about 5 folds increases more than the control group. For MicroRNA-155 there were about 2 folds increases in PE group more than the control group. The present results were in agreement with those presented by Gan et al. [18] who reported that MiRNA-210 and MiRNA-155 were up-regulated in serum of PE pregnancies, and suggested a potential association between these two MiRNAs and the pathogenesis of PE. Many researchers reported that MiRNA-210 was over-expressed in Preeclampsias as stated in [13,19,20] and [21] which were in agreement with our results.

Pineles et al. were the first researchers to identify increased expression of specific placental MiRNAs in Preeclampsia with and without SGA. They reported differential expression in MiRNA-210 between Preeclampsia and the control groups, and that MiRNA-210 was specific for regulation of transcription [20]. Both MiRNA-155 and MiRNA-210 were up-regulated in PE which had complications on the kidneys, and were also up-regulated in renal cell carcinoma [22]. In another study, MiRNA-210 was involved in the molecular response in hypoxic kidney lesions and attenuated hypoxia-induced renal tubular cell apoptosis by targeting hypoxia inducible factor (HIF-1α) [23].

Table 1 clarifies that there are no significant differences between the two groups as regards age and parity. There is a high significant increase in MiRNA-210 relative expression in PE group (5.84 ± 3.38) more than control group (1.02 ± 0.06) with p = 0.0001. Also, there is a high significant increase in MiRNA-155 in PE group (2.92 ± 0.48) more than control group (1.40 ± 0.35) with p = 0.001. There are significant decreases in gestational age and fetal birth weight in PE group versus the control group. The systolic blood pressure, diastolic blood pressure, mean blood pressure, urine albumin, ALT, and AST are significantly increased in the PE group compared to the control group.

In this study, the number of Cesarean section deliveries increases significantly in the PE group; it was (53.33%), compared to the control group which was (35%).The Ministry of Health and Populations in Egypt; reported that (50.8%) of all deliveries were by CS [24]. A study performed at the Maternity Hospital, Ain Shams University, reported the CS rate of (43.86%) in both the high risk and the emergency units which included the PE patients [25].

Table 2 shows the inverse significant correlation between MiRNA-210 with gestational age and fetal birth weight in the PE group. Also, there is a direct significant correlation with urea, and high significant direct correlations between MicroRNA-210 and systolic, diastolic, mean arterial blood pressure and creatinine in the patients with Preeclampsia which suggested more deterioration of cases with higher MiRNA-210 in both mother and fetal parameters.

Considering the total number of subjects in the study, Table 3 shows the high significant inverse correlation between MicroRNA-210 with gestational age and fetal birth weight, also there are high direct significant correlations with systolic, diastolic, mean blood pressure, ALT, AST, creatinine, urea and urinary albumin.

The results in Table 4 shows that in the Preeclampsia group there are non-significant correlations between MicroRNA-155 with GA, parity, systolic, diastolic, mean ABP, ALT, AST, creatinine, urea, urine or serum albumin and lastly fetal birth weight. Thus, MicroRNA-155 could not be used as a prognostic biomarker for severity of Preeclampsia.

Furthermore, the results in Table 5 clarifies the high significant difference in mean ABP, gestational age at delivery, fetal birth weight, MicroRNA-210 and MicroRNA-155 between mild PE, severe PE and control groups. Mean-ABP levels are (109.95 ± 4.26) in mild PE subgroup, (133.28 ± 7.67) in severe PE subgroup and (84.44 ± 8.08) mmHg in control group with p = 0.0001. Gestational ages at delivery are (37.75 ± 1.35), (35.00 ± 4.02) and (38.6 ± 0.94) weeks in mild, severe PE and control groups respectively, with p = 0.001. Fetal birth weight mean levels are (2975.0 ± 169.8), (2448.8 ± 548.5) and (3480.0 ± 308.8) grams in mild PE, severe PE and control groups respectively with p = 0.003. MicroRNA-210 mean levels were (3.21 ± 1.84), (7.63 ± 2.93) and (1.02 ± 0.06) relative expressions in mild, severe PE and control groups respectively with p = 0.0001. MicroRNA-155 mean levels were (3.00 ± 0.51), (2.87 ± 0.48) and (1.40 ± 0.35) relative expressions respectively with p = 0.01. In severe PE subgroup the level of MicroRNA-210 is more than 2 folds higher than in the mild PE subgroup. On the other hand, there was no significant difference between MicroRNA-155 levels in mild and severe PE subgroups with p = 0.466. These direct high significant correlations between MicroRNA-210 with the clinical and biochemical parameters of severity of Preeclampsia proposed considering MicroRNA-210 as a prognostic biomarker for Preeclampsia severity. This finding is consistent with that reported by Kelsey et al. in their review that MicroRNA-210 is up-regulated in PE and the multitude of MicroRNA-210 functions could affect different pathways during PE, such as mitochondrial dysfunction, angiogenesis, and immune system [26].Yang et al. found MicroRNA-155 and IL-17A to be up-regulated in late onset PE placentas and serum [27]. Also, our results agrees with the study performed by Anton et al. who stated that MicroRNA-210 was up-regulated in PE and can be considered as a serum biomarker for PE [19].

Table 6 demonstrates that severe PE subgroup has significant higher systolic, diastolic, mean ABP, urine albumin, creatinine and MicroRNA-210; non-significant difference in urea, ALT, AST, serum albumin, and MicroRNA-155, and significant reduced GA and fetal birth weight compared with mild PE subgroup.

Munaut et al. in their study postulated that four circulating MicroRNAs (MiR-210-3p, MiR-210-5p, MiR-1233-3p, and MiR-574-5p) were differentially expressed in the sera of women who developed PE compared to controls. This confirms the possible pathophysiological role of MicroRNAs in PE and might also provide a new clinical strategy for identifying women who are at risk of developing PE [28].

Also, in agreement with our study Gan et al. suggested that elevation of MiRNA-210 and MiRNA-155 expression in the serum was associated with the development of PE. Their findings may provide an early diagnosis method to identify women who are at risk of developing PE [18]. In their research, they connected elevated MicroRNA-210 and MicroRNA-155 with clinical sequel of PE and related both to PE etiology and pathophysiology. Our result confirms what was previously reported by Gan et al. regarding MicroRNA-210 to be a predictor of the severity of PE. Although MicroRNA-155 expression is up-regulated in Preeclampsia group in our study, there is a non-significant difference in MicroRNA-155 between mild and severe subgroups of Preeclampsia, which was not consistent with that reached by Gan et al. [18]. Perhaps this is due to the difference in time of collecting samples as they took the samples early in pregnancy and we took the samples at the time of delivery.

It is well recognized that no single molecule or signaling pathway could be responsible for the occurrence of the complex Preeclampsia syndrome. Maintaining homoeostasis in many organs, including the placenta, is established by MicroRNAs through targeting a large number of genes and participating in various cellular events. The identification

of dys-regulated MicroRNAs in preeclamptic placentas and the clarification of gene networks that are regulated by those MicroRNAs would likely be novel steps in understanding the pathogenesis of such compromised pregnancies [12]. The stable properties, as well as the early differential patterns of plasma MicroRNAs in Preeclampsia patients, as shown in the study of Gunel et al., strongly suggested the significant potential of using these molecules in the non-invasive prenatal diagnosis of Preeclampsia [29]. A recent study confirmed that (MiR-210, MiR-155, MiR-650, MiR-215, MiR-21) were up-regulated, and (MiR-18a, MiR-19b1) were down-regulated in women with PE compared to the control group, and between women with severe PE compared to those with mild PE; it confirmed the contribution of MicroRNAs to PE pathogenesis, as well as being predictors of the severity of PE [30].

4. Conclusions

Our study confirmed the elevation of MicroRNA-210 and MicroRNA-155 in the serum of Preeclampsia pregnancies compared to the healthy pregnancies. Another finding was the significant direct correlation of MicroRNA-210 with the severity of Preeclampsia.

5. Recommendations

More studies are needed to clarify the role of the elevated MicroRNA-210 and MicroRNA-155 in PE and their relation to etiology, pathophysiology, severity of the PE; and if MicroRNA-210 can be used as a diagnostic biomarker to identify women who will proceed to severe PE.

Acknowledgement

Thanks to Dr. Laila Rashed, Professor of Biochemistry, Faculty of Medicine, Cairo University, for her help in performing the biochemical analysis of all parameters in this study.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. We have not received any grant.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.preghy.2019.05.010.

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