Platelet Parameters in Healthy and Pathological Pregnancy

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Changes in platelet count (PLT) are very important during pregnancy. Many platelet disorders occur during pregnancy and a reduction in PLT is the most common hemostasis abnormality identified, and this has important implications for mother and foetus. Many of these disorders share clinical and laboratory features, making accurate diagnosis difficult. The aim of this study was to establish reference intervals of platelet parameters for some of the more important pathologies associated to pregnancy (pre-eclampsia, gestational diabetes, autoimmune disorders, viral infections) using the automated hematology analyzer Sysmex XE-2100 and to evaluate the difference between healthy and pathological pregnancy. We enrolled in our study 100 pregnant women in the third trimester of

pregnancy. The parameters analyzed included PLT, platelet distribution width, and mean platelet volume (MPV). We found statistically significant difference in PLT in pre-eclampsia, autoimmune disorders, and viral infections. Our results demonstrated also a statistically significant difference in MPV in pre-eclampsia and gestational diabetes. Our results allow the clinicians to detect hematologic change by simple complete blood count useful for the management of the pathological pregnancies. In conclusion, the overall picture of platelet disorders is extremely variegated, leading to numerous diagnostic and therapeutic problems whose solutions require close collaboration between clinicians and laboratory specialists. *J. Clin. Lab. Anal.* 26:41–44, 2012. © 2012 Wiley Periodicals, Inc.

Key words: blood cell count; gestational diabetes; platelet; pregnancy; pre-eclampsia; reference values; thrombocytopenia

INTRODUCTION

Changes in platelet count (PLT) are very important during pregnancy. In fact, during normal pregnancy changes in blood coagulation and fibrinolysis create a state of hypercoagulability (1, 2). PLT play a pivotal role in the initiation of the coagulation process. There is also evidence that platelets play a substantial role in the pathogenesis of pre-eclampsia (3–5).

Many platelet disorders occur during pregnancy (6) and a reduction in PLT is the most common haemostasis abnormality identified; this has important implications for mother and foetus, and not inconsiderable anxiety for the doctor and patient (7–9). Thrombocytopenia occurs in up to 10% of pregnancies and is the second haematological disorder after anaemia. Thrombocytopenia in the pregnant patient may result from a number of causes (10, 11). In most cases, thrombocytopenia is gestational or incidental: this “physiologic” decrease in platelets occurs in the third trimester (12–14). These observations suggest

that pregnancy is associated with a mild and generally unappreciated decrease in the circulating PLT.

However, thrombocytopenia in pregnancy may occur secondary to a variety of causes, ranging from benign disorders, such as gestational thrombocytopenia, to syndrome associated with significant morbidity, such as immune thrombocytopenia that may complicate pregnancy and its management (15, 16). Many of these disorders associated with thrombocytopenia share clinical and laboratory features, making accurate diagnosis difficult (17, 18). In most cases, the underlying cause of thrombocytopenia

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may be diagnosed when the time of onset, clinical manifestations, and laboratory studies are considered together.

In a previous study (12), we established the reference intervals of platelet parameters during the three trimesters of normal pregnancy using a fully automated hematology analyzer.

The aim of this study was to establish reference value of platelet parameters in the third trimester of pregnancy in some of the more important diseases associated to pregnancy (pre-eclampsia, gestational diabetes, autoimmune disorders, viral infections), using the automated hematology analyzer Sysmex XE-2100 (Sysmex Corporation, Kobe, Japan) and to evaluate the difference between healthy pregnancy and these diseases associated with thrombocytopenia in order to investigate whether any haematological changes detectable by simple complete blood count can improve the pathophysiology, differential diagnosis, and management of these disorders.

MATERIALS AND METHODS

Specimens

We enrolled in our study a total of 100 pregnant women in the third trimester of pregnancy. The women during pregnancy were affected by the following diseases: pre-eclampsia, gestational diabetes, autoimmune disorders, and viral infections (HIV, HCV) (Table 1).

One hundred healthy pregnant women in the third trimester of pregnancy were enrolled as a control group.

Automated PLT Count

The platelet parameters were measured by the Sysmex XE-2100 fully automated hematology analyzer on venous sample collected in K₃EDTA. The specimens were analyzed within 1 hr from venesection. Sysmex XE-2100 for the platelet measure employs both the impedance and the optical method; however, platelets were measured once with each mode. In impedance measurement, cells are passed one after the other through a capillary opening. The passing cell produces an electrical resistance, and thus an electronic signal that is proportionate to its volume. Optical (fluorescent method) platelets' RNA is stained

and then platelets are recorded flow cytometrically by means of semi-conductor laser technology. The parameters analyzed included PLT, platelet distribution width (PDW), and mean platelet volume (MPV). Observation based on the MPV were considered valid only if the specimens were analyzed within 1 hr from venesection, to avoid the problems occurring when EDTA collected samples are analyzed with impedance systems.

Statistical Analysis

The reference intervals of PLT, MPV, and PDW in the third trimester of pregnancy are calculated using the nonparametric summary statistics. Reference intervals are presented as mean $\pm$ 2SD. Differences of platelet parameters between normal and pathological pregnancy are tested using the analysis of variance and *t*-test with Bonferroni correction. Significance was assumed at $P < 0.0001$. All statistical analysis was performed with SPSS software for Windows version 10.07 (SPSS, Chicago, IL).

RESULTS

We established the platelet parameter reference intervals of pregnant women in the third trimester of pregnancy in studied diseases. Then, we made the comparison of platelet parameters between healthy pregnant women and pregnant women with PE, gestational diabetes, autoimmune disorders, and viral infections.

We did not find a statistically significant difference ($P < 0.0001$) of platelet parameters between the normal and pathological pregnancy for all the parameters, but only for PLT and MPV. Particularly, pregnant women with PE, autoimmune disorders, and viral infections showed a decrease in the PLT compared with the group of normal pregnant women. Pregnant women with PE and gestational diabetes showed a statistically significant increase in MPV. The other platelet parameters showed differences, but were not statistically significant (Table 2).

DISCUSSION

Platelet disorders is a frequent finding during pregnancy, and they have been more commonly diagnosed in pregnant women in the last 20 years because PLTs are included with the automated blood cell counters (19). The PLT is usually between $110 \times 10^9/L$ and $150 \times 10^9/L$, but can be lower and returns to normal after delivery.

The most common coagulation abnormality is thrombocytopenia, but in most cases (more than 75%) this is gestational or incidental thrombocytopenia with no clinical significance and probably owing to hemodilution or to increased platelet destruction occurring through

TABLE 1. Population Analyzed

Disease	<i>N</i> = 100
Pre-eclampsia	46
Gestational diabetes	25
Autoimmune disorders	11
Viral infections (HIV, HCV)	18

N, total number of pregnant women.

TABLE 2. Comparison of Platelet Parameters Between Normal and Pathological Women in the Third Trimester of Pregnancy

	Healthy pregnancy	Pre-eclampsia	Gestational diabetes	Autoimmune disorders	Viral infection (HIV, HCV)
Platelet ($10^3/\text{ml}$)	212.09 $\pm$ 135.44*	192 $\pm$ 56.3*	258 $\pm$ 67.1	203 $\pm$ 63.5*	220 $\pm$ 4.1*
MPV (fl)	8.3 $\pm$ 1.1	11.95 $\pm$ 1.2*	11.92 $\pm$ 1.9*	8.85 $\pm$ 0.9	9.8 $\pm$ 0.9
PDW (fl)	14.14 $\pm$ 4.98	15.13 $\pm$ 2.7	13.6 $\pm$ 1.7	13.5 $\pm$ 3.2	10.9 $\pm$ 1.8

Data are expressed as mean $\pm$ 2 SD. *P*-values with asterisk (*) highlight significant differences between groups ($P < 0.0001$). PLT, platelet count; MPV, mean platelet volume; PDW, platelet distribution width.

immune and nonimmune mechanisms. A differential diagnosis from other causes of thrombocytopenia in the adult is, however, necessary.

These disorders must be recognized with accuracy, precision, and quickly. In this way, we can find out also the preclinical sign of the pathologies and we can make diagnosis quickly and avoid severe complications for the mother and the foetus. It is very important that hematologists and obstetricians are aware of these differences, because deviations from reference intervals could indicate the onset of complications. Even with its wide differential diagnosis, the cause of platelet disorders during pregnancy can usually be determined with a thorough history, physical examination, and directed laboratory studies (20,21). The challenge to the clinicians is to weigh the risk of maternal and foetal bleeding complications against the benefits of diagnostic tests and interventions.

This study defines specific reference range for platelet parameters (PLT, PDW, MPV) in healthy pregnant women and in the more frequent diseases (PE, gestational diabetes, autoimmune disorders, and viral infections) associated with platelet disorders during pregnancy.

Several studies have reported data about the platelet parameters during pregnancy (4,5,22,23), but to our knowledge this is the first study that determines reference intervals in pregnant women in the third trimester of pregnancy with PE, gestational diabetes, autoimmune disorders, and viral infections using the automated haematology analyzer Sysmex XE-2100.

We compared these reference intervals with reference intervals of normal pregnant women in the third trimester of pregnancy. The comparison between the two groups showed a statistically significant difference between healthy pregnant women and pregnant women with all the diseases studied. According to previous studies (24,25), pregnant women with PE have lower PLT and higher MPV. Thrombocytopenia associated with PE has pathogenic similarities with thrombotic thrombocytopenic purpura; the characteristic feature is the nonimmune platelet consumption. The high MPV associated with PE is caused by an increase in the heterogeneity of human platelet caused by an increased number of larger platelets. Larger platelets seem to be more reactive than the smaller ones (26). A large platelet can be a concomi-

tant symptom of acquired disease. Pregnant women with gestational diabetes did not show any statistically significant difference in the PLT, but we found that MPV was statistically significant higher than in healthy pregnant women. Other studies demonstrated that platelet activity is enhanced in PE and gestational diabetes, and it may play an important role in the pathogenesis and development (24,25). We also found that pregnant women with autoimmune disorders have lower PLT, probably secondary to platelet destruction owing to antiplatelet antibodies, circulating immune complexes, or other causes (27,28). Also, in pregnant women with viral infections, PLT is statistically significantly lower than in healthy pregnant women. The other platelet parameters showed differences, but were not statistically significant.

In conclusion, the overall picture of platelet disorders is extremely variegated, leading to numerous diagnostic and therapeutic problems whose solutions require close collaboration between clinicians and laboratory specialists. In fact, thrombocytopenia usually is a benign condition. Some patients, however, will have chronic medical disorders or pregnancy-induced conditions that require further evaluation and therapy. The reference intervals and the differences that we have found in PLT and MPV between healthy and pathological pregnant women can be helpful in the differential diagnosis and in the management of complicated pregnancies.

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