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RESEARCH ARTICLE
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ROLE OF CORTICOSTEROIDS IN TREATMENT OF LOW-PLATELET DISEASES IN PREGNANT WOMEN

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Abstract

Background and Objectives : Assessment of pregnant women associated with thrombocytopenia(incidence – proposed risk factors – different causes of thrombocytopenia – maternal and neonatal complications) as it is an important disorder and considered a second haematological disorder during pregnancy after iron-deficiency anaemia . It is defined as aplatelet count below < 150,000/mm^3 .This study compared two groups of participants to prove that dexamethasone is relatively safe and cost-effective in elevating of platelet count in Hellp syndrome.

Methods : This was a statistical descriptive study ,also experimental randomized controlled trial to investigate the role of dexamethasone in treatment , was conducted in the hospital of Obstetrics and Gynecology,Aleppo,Syria over 2 years.the participants were 600 women with thrombocytopenia, 210 of them who underwent dexamethasone and observation , platelet count was reassessed after 12-24-48 hours via CBC.

Results : incidence was 7.31%, different causes were: Gestational 58% - Hypertension-related diseases 23.5% - Idiopathic Thrombocytopenia Purpura 2,8% - Drugs 2.5% - Viral 2.2% - Bone Marrow Diseases 1.2% - Acute fatty Liver Of Pregnancy 0.5% - Heamolytic Ureamic Syndrome 0.3% - Antiphospholipid Antibodies Syndrome 0.3% - Systemic Lupus Syndrome 0.2%, Severity was: Mild 83.5% - Moderate 14.3% - Severe 2.2%,presence of risk factors: Hypertension 23.5% - Diabetes Mellitus 1.8% - Smoking 11.2% - Age 20-24 yrs 25.3% .Maternal Complications were: Blood 24.5%,Plasma 14.7%,Platelet 4% Transfusion – Labour Induction 1% - Placental Abruption 3.2% - Placental Previa 5.7% - Purpura 1.3% - Ecchymosis 2.2% - Vaginal Bleeding 17% - Drainage Bleeding 19.8% - Haematuria 1.2% - Dissaminated Intravascular Coagulation 1.3%. Fetal and Neonatal Complications: Apgar Scores at 1-5 minute less than 7 was 7.2%,2.2% , preterm Delivery 22.3% , Premature Rupture Of Membrane 2.2% , Neonatal Death 0.5% .It showed beneficial of dexamethasone in elevating platelet count accordin to cause of thrombocytopenia as it was safe and cost –effective in HELLP Syndrome and it did not benefit in bone marrow diseases.

Keywords : Thrombocytopenia , Pregnancy , Dexamethasone

INTRODUCTION:

Thrombocytopenia is one of the most popular medical problem during pregnancy which forms challenges on patients and doctors together, as it makes serious and detrimental complications on mothers and babies unless an appropriate treatment is done.
Thrombocytopenia is defined as platelet count below 150.000/mm^3 .
It is classified into 3 grades according to severity as:
Mild Form : 150.000-100.000/mm^3 .
Moderate Form : 100.000-50.000/mm^3 .
Severe Form : less than 50.000/mm^3 .
It is results from increase in peripheral destruction of platelets or loss manufacturing of platelets from bone marrow .
It usually occurs physiological (not pathological) thrombocytopenia during pregnancy by 10% of normal basaline count in prepregnancy, usually occurs in the third trimester of pregnancy , and this may be back to either more haemodilution or excessive destruction of platelets in peripheral circulation .

Physiological and Morphological Sight :

Platelet is an anucleus cell, discoid form, diameter 2-3 micron, size 5-7 vimtolittre.
It forms from sequestration of megakaryocytes in bone marrow .
It contains obvious particles(alpha- delta) .
The cellular membrane of platelet is the site of different coagulation factors to cascade hemostasis events , for that the bleeding from platelet deficiency or functional disorders is severe as coagulation factors don't perform their functions well although they mayn't loss in quantity .

Hemostasis :

Is defined as stopping haemohrrage from injured vessels, starts by forming a clot consisting of platelets at the beginning and then strengthened by participating of coagulation factors which activate postinjury leading to stability of the clot and consolidation with fibrin fibers, after that an opposite mechanism(fibrinolytic mechanism) is activated to prevent excessive clot formation and save balance between coagulation and the normal state of blood inside vessels which is liquid .
Hemostasis is required collaboration,reinforcement and overlap of 3 factors as the following :
1-safety of blood vessels ,especially endometrium .
2-plateles ,the most important factor in hemostasis .
3-coagulation factors .

Functions of platelets :

The most important function is forming clots in sites of endometrial injuries through these mechanisms (Aggregation – Adhesion – Secretion – Shrink) .
Tests of platelet functions : Bleeding Time(BT) .
Different Causes of Thrombocytopenia :

Gestational Thrombocytopenia(GT)

Pathophysiology:unknown exactly,but maybe due to excessive activation of platelets in placental circulation leading to excessive peripheral destruction .
Diagnosis: more than 20 gestational age, no previous history of thrombocytopenia, mild , regress spontaneously after 2-12 weeks of delivery .
Treatment: observation .

Hypertension-associated disorders

Gestational/ Transient Hypertension , Mild/ Severe Pre-eclampsia/ Eclampsia/Pre-eclampsia Superimposed On Chronic Hypertension .

HELLP Syndrome
Anaemia + Elevation in liver enzymes + Thrombocytopenia .

Immune Thrombocytopenia Purpura(ITP)
Pathophysiology: Autoimmune antibodies IgG
Diagnosis:persistent deficiency of platelets less than 100.000/mm^3 after excluding systemic and pharmacological causes ,the standard diagnosis is bone marrow puncture .
Treatment: prednisolone 60 mg/day .

Thrombotic Thrombocytopenia Purpura(TTP)
Diagnosis:autoantibodies destroy ADAMTS13 enzyme which is responsible for cleavage of V.W.F,leading to platelet aggregation and thrombocytopenia .
Treatment: plasma phoresis and exchange by fresh frozen plasma .

Hemolytic Uremic Syndrome
Acute Fatty Liver Diseases Of Pregnancy
Pathophysiology:recessive inherited mitochondrial abnormalities of fatty acid oxidation , B-oxidase enzyme deficiency .
Diagnosis : by presence of 6 or moer of Swansea Criteria :
1-vomiting2-abdominal pain 3-polydipsia/polyuria 4-encephalopathy 5-hyperbilirubin>14mmol/l 6-hypoglycemia<4mmol/l 7-uremia>340micromol/l 8-elevated WBC>11 $*10^9$ /l 9-ascite 10-elevation AST/ALT >42 unit/l 11-amonia>47micromol/l 12-creatinine>150micromol/l 13-PT>14second 14-liver biopsy: microvesicular steatosis .

Systemic Lupus Erythematous (SLE)
Pathophysiology : chronic inflammatory immune disease .
Diagnosis: 4 criteria of American Rheumatism Association Criteria as the following :
1-facial butterfly rash 20photosensitivity of skin rash 3- dicoid lupus 4- oral or nasopharyngeal ulceration 5-arthritis:non-erosive ,migratory of two or more peripheral joints 6- serositis: pleurisy,pericarditis 7- renal problems: proteinuria more than 500mg/day 8-neurological problem: psychosis or convulsions 9- haematological problems: haemolytic anaemia,leucopenia less than $4*10^9$ /l , lymphopenia less than $1,5*10^9$ /l or thrombocytopenia less than $100*10^9$ /l 10-Anti-DNA,Anti-nuclear Antibodies(ANAs) , chronic false positive syphilis serology for more than 6 months
Treatment: predinisolon during pregnancy to prevent activity of disease

Antiphospholipid Antibodies Syndrome (APA)
Diagnosis:1 clinical+ 1 laboratory of criteria :
Clinical :
1-vascular thrombosis : arterial/ venous .
2-3 or more consecutive miscarriage less than 10 weeks
3-One or moer fetal death more than 10 weeks .
4-one or more preterm delivery less than 34 weeks due to pre-eclampsia or placental insufficiency .

Laboratory :
1-Anticardiolipin Antibodies in medium or high titre on at least 2 occasions more than 6 weeks apart .
2-Lupus Anticoagulant on at least 2 occasions more than 6 weeks apart .
3-Anti-B2-glycoprotein-1 Antibodies .
Treatment: Aspirin – Heparin

METHODS :

This study was statistical descriptive , which designed to evaluate pregnant women associated with thrombocytopenia ,also experimental (RCT) to evaluate the efficacy of dexamethasone , in Department Of Obstetris and Gynecology ,Faculty of Medicine ,Aleppo University comprising of 600 women with thrombocytopenia ,210 women of whom undertaken to evaluate efficacy of dexamethasone after 12- 24 -48 hours . The study was done between 29-7-2021 and 31-1-2023 .

A detailed medical history ,physical examination , laboratory tests (CBC,AST,ALT,LDH,urea, creatinine,coagulation tests) to identify thrombocytopenia and diagnosis the different causes of them. We had too more laboratoey tests and haematological referrals to assign causes of thrombocytopenia in some complicated cases(peripheral blood smear-HBSAg-HCV- Widal/Wright test – FOB- VitB12- Urinalysis – Proteinuria- ferritin). Women were eligible to enter the study ,written consent was obtained prior to any assessments .

Criteria for exclusion were :

dexamethasone use in the last 15 days , chronic use of corticosteroids,chronic diseases such as chronic liver, patients unable to consent(coma-critical clinical condition)and without accompanying persons that may consent to study participation .

The follow-up interval was 2 months after discharge

Attempts to complete follow-up were undertaken by telephone,what's up , and in person .

The dosage of dexamethasone was taken in this study 12 mg , 12 hours interval , two dosages .

The follow-up after taken dexamethasone and observation was by CBC after 12-24- 48 hours .

RESULTS

The incidence of thrombocytopenia in Obstetrics and Gynecology University Aleppo Hospital was 7.31% .

Severity of Thrombocytopenia was as the following : mild 83.5%, moderate 14.3% , severe 2.2% (table 1).

The commonest cause of thrombocytopenia was Gestational Thrombocytopenia (GT)58% ,followed by Hypertension –related diseases and HELLP Syndrome 23.5%(table 2) .

The commonest maternal complications were blood transfusion 24.5% , plasma transfusion 14.7%, placental abruption 3.2% , vaginal bleeding 17% , scar bleeding 16.3% , haematuria 1.2%(table 3).

The commonest fetal and neonatal complications were apgar score at 1-5 minutes less than 7 (7.2%,2.2%), preterm delivery 22.3%(table 4).

It's noticed of beneficial of dexamethasone in elevation of platelet count after 12 hours with mean was $39.4*10^9$ /mm, after 24 hours with mean was $49*10^9$ /mm and after 48 hour,the mean was $65*10^9$ /mm , so it's recommended that dexamethasone as it's safe and cost-effective in platelet count elevation, espically with HELLP Syndrome .

Dexamethasone didn't benefit in improvement of platelet count with bone marrow diseases .

Table5 reveals significant at p-value <0.05, clinical and laboratory importance at more of 25% of baseline value , Preson correlation between values of platelet counts before and after dexamethasone and observation.

Table1:Severity of theombocytopenia	Case number	percentage
Mild	501	**83.5**
Moderate	86	**14.3**
Severe	13	**2.2**
Total	600	**100**

Table2:Causes of thrombocytopenia	Case number	Percentage
Gestational Thrombocytopenia	348	**58**
Gestational Hypertension	49	**8.2**
Mild Ec-clampsia	42	**7**
Severe Ec-clampsia	26	**4.3**
Ec-clampsia	7	**1.2**
Chronic Hypertension	8	**1.3**
HELLP Syndrome	11	**1.8**
Acute Fatty Liver Diseas Of Pregnancy	3	**0.5**
Immune Thrombocytopenia Purpura (ITP)	17	**2.8**
Bone Marrow Diseases	7	**1.2**
Thrombotic Thrombocytopenia Purpura (TTP)	0	**0**
Hemolytic Ureamic Syndrome (HUS)	2	**0.3**
Systemic Lupus Erythematous (SLE)	1	**0.2**
Antiphospholipid Antibodies (APA)	2	**0.3**
Pharmacological	15	**2.5**
Viral	13	**2.2**
Others	48	**8**
Total	600	**100**

Table3:Maternal complications	Case number	Percentage	P-value
Blood Transfusion	147	24.5	**0.001**
Plasma Transfusion	88	14.7	**0.001**
Platelet Transfusion	24	4	**0.03**
Placental Previa	34	5.7	**0.3**
Placental Abruption	19	3.2	**0.1**
Labour Induction	6	1	**0.13**
Vaginal Bleeding	102	17	**0.2**
Hematuria	7	1.2	**0.01**
Ecchymosis	13	2.2	**0.001**

Table4:Neonatal Complications	Case number	Percentage	P-value
Apgar score less than 7 at minute 1	43	7.2	**0.01**
Apgar score less than7 at minute5	13	2.2	**0.02**
Preterm Delivery	134	22.3	**0.2**
P.Prom	13	2.2	**0.2**
IUGR	10	1.7	**0.06**
IUFD	26	4.3	**0.3**
Neonatal Death	3	0.5	**0.3**

It was considered that mean platelet count elevation by more than 25% of basal value before taken dexamethasone as a criteriae to evaluate improvement in platelet count clinically and laboratory.
It was considered that p-value less than 0.05 as a statistical significant value in our study .
Observation was done by CBC .

Observation was done after 12-24-24 hours after the first CBC was documented.

Platelet Count									
Taken Dexamethasone	Elevated Case number	percentage	Decreased Case number	Percetage	*P-value	Statistical significance	Mean elevated Platelet	Percentage**	**Clinical and Laboratory Significance**
After 12 hours									
Yes	85	81	13	12.4	0.001	significant	39.400/mm3	50	**significant**
No	26	24.5	66	62.9	0.012	significant	4.000/mm3	3.4	**Non-significant**
After 24 hours									
Yes	51	48.6	11	10.5	0.012	significant	49.000/mm3	61.2	**significant**
No	21	20	27	25.7	0.001	significant	12.000/mm3	10	**Non-significant**
After48 hours									
yes	29	27.6	5	4.8	0.013	significant	65.000/mm3	86	**significant**
No	7	6.7	10	9.5	0.01	significant	3.000/mm3	2.8	**Non-significant**
P-value< 0.05*									
Pcentage of mean elevated platelet must be more than 25% of baseline value **									

Table6: reveals different causes of thrombocytopenia ranked ascendly according to percentage of mean elevated platelet count after undertaken dexamethasone

12 hours	24 hours	48 hours
>100%	>100%	**>100%**
Acute Fatty Liver of Pregnancy	HELLP Syndrome	**HELLP Syndrome**
HELLP Syndrome	Severe Ec-clampsia	**100-75%**
100-75%	100-75%	**Hus**
Ec-clampsia	Acute Fatty Liver of Pregnancy	**75-50%**
75-50%	75-50%	**Gestational Thrombocytopenia**
Drug	viral	**DIC**
Viral	50-25%	**Ec-clampsia**
50-25%	ITP	**50-25%**
ITP	Hus	**ITP**
<25%	Drug	**<25%**
Bone Marrow Diseases	<25%	**Bone Marrow Diseases**
	Bone Marrow Diseases	**Viral**

DICUSSION

This is the first study in the Hospital of Obstetrics and Gynecology at Aleppo University to evaluate incidence,different causes of thrombocytopenia and role of dexamethasone in treatment.The study revealed that dexamethasone is relatively safe and cost-effective in improvement of platelet count in HELLP Syndrome and did not benefit in ITP and bone marrow diseases .It is important to identify the cause of thrombocytopenia as the complications and treatment varies according to its cause .

CONCLUSION

The incidence of thrombocytopenia was 7.31%, the most common cause was Gestational Thrombocytopenia, the most maternal complication was blood transfusion ,the most common fetal complication was preterm delivery,dexamethasone was relatively safe and benefit in HELLP Syndrome but didnot never benefit in bone marrow diseases.

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Conflicts of interest

There are no conflicts of interest

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