Study of Hematological Profile in Healthy Pregnant and Non-Pregnant Women in Erbil City

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Abstract:

Background and objective: Pregnancy is characterized by profound changes in almost every organ system to accommodate the demands of the fetoplacental unit. Hematologic system is one of these systems and should adapt in a number of ways. This study, attempted to assess the effect of pregnancy on the hematological indices and compare these indices at different stages of pregnancy with non- pregnant women.

Methods: A cross sectional study was conducted in different medical health centers in Erbil, Iraq from 1st April 2016 to 31st January 2017. (139) apparently healthy pregnant women aged from (16-46) years, were recruited into the study as a case group, and (104) healthy non pregnant aged from (19-46) years as a control group. Venous blood was collected from each subject. Complete blood count was estimated by automated hematological analyzer.

Results: Study group showed statistical difference in RBC count, hematocrit, MCH, WBC count, monocyte %, granulocyte % and platelet count at ($p< 0.0.5$) between pregnant and non pregnant women. Significant differences were observed in some of the hematological parameters among the three TMs.

Conclusion: Normal pregnancy can alter hematological indices and also affected by different pregnancy stages.

Keywords: Pregnancy, physiological changes, hematological parameters, trimesters.

Introduction:

Many physiological changes occur during pregnancy, which may appear to be pathological in non-pregnant state [(1)]. Normal pregnancy is characterized by profound changes in almost every organ and systems to accommodate the demands of fetoplacental unit [(2)]. The importance and significance of the knowledge of hematological parameters in advanced pregnancy stems from the fact that the hematological profile of pregnant woman has an impact on pregnancy and its outcome, and between the hematological indices that affected by pregnancy are red blood cell count, hematocrit, total and differential white blood cell count and platelet count [(3, 4)].

The most common hematological indices are the indicators of hemoglobin concentration. Low hemoglobin in the blood is widely identified as a hematological abnormality and it is associated with adverse pregnancy outcome [(5)].

The values of these parameters, which includes packed cells volume (hematocrit), red and white blood cells counts, platelet count and differential

leukocytes count, enables the health workers to reach one of several diagnosis and decisions.

The fact remains that some hematological parameters are bound to show alteration in certain conditions, including pregnancy. For example, hematocrit value employed to evaluate anemic condition, platelet count value employed to monitor the cause of excess bleeding, leukocyte count is indicator to track several disease conditions [6].

During normal pregnancy, leukocyte count has been shown to increase progressively throughout the period of gestation. Leukocyte count ranges of 5000/microliter to 12000/microliter have been reported [7].

The total blood volume also increases by about 1.5 liters, mainly to supply the demands of the new vascular bed and to compensate for blood loss occurring at delivery [8].

In normal pregnancy the hematological indices of an individual to a large extent reflex their serial health and many studies such as Osonuga *et al*. and Shaw *et al.* have identified the hematological indices of the pregnant women as one of the factors affecting pregnancy [9, 10].

Anemia among women of reproductive age is so common. Even when anemia is noted early in pregnancy and treated promptly, there is an increased risk of preterm birth. More severe cases of anemia (Hb < 8gm/dl) are associated with greater risk of preterm birth and low birth weight [11].

There are also quality of life issues associated with maternal anemia that are comparable to those seen in individuals with serious chronic diseases such as difficulty in concentration, cognition, disturbed mother – infant interactions and depression. Postpartum fatigue and reduced immune function associated with increased risks for infection were also shown to have a relationship with anemia [11].

Aims of the study:

1. To assess the changes in hematological parameters in pregnant women in comparison with non-pregnant controls.
2. Examination of these hematological parameters across the three trimesters of pregnancy.
3. Evaluate each type of hematological indices separately in pregnant & control women.

Methods:

Participants:

With the approval of the local ethics committee in the ministry of Health and the medical ethics committee in the college of Medicine, a cross sectional study was conducted from 1st April 2016 to 31st January 2017 in different medical health centers in Erbil city. The study included (243) women aged from (16-46) years. One hundred thirty nine (139) apparently healthy pregnant women on their antenatal visit aged from (16-46)years, were recruited into the study as a case group, and one hundred four (104) healthy non pregnant volunteers women who are relatives to pregnant women aged from (19-46) years as a control group.

The medical health centers were: Minara, Kurdistan, Nazdar, Bamarny, Malafandi and Tayrawa health centers in Erbil. In healthy pregnant women, forty four (32%) of them were in first trimester (1st TM), forty nine (35%) in second trimester (2nd TM) and forty six (33%) in third trimester (3rdTM) as in figure (1).

Women with any of the following conditions were excluded from the study: known cases of hemolytic anemia, bleeding disorders, active bleeding from any site; blood pressure ≥ 140/90mmHg; major surgery or road traffic accident in the last one year,

and women with known splenomegaly and haemoglobinopathy, smoked or with underlying chronic illness (renal, diabetes mellitus, with acute or chronic infection). In addition, women on nonsteroidal anti-inflammatory drugs such as aspirin and on heparin were also excluded.

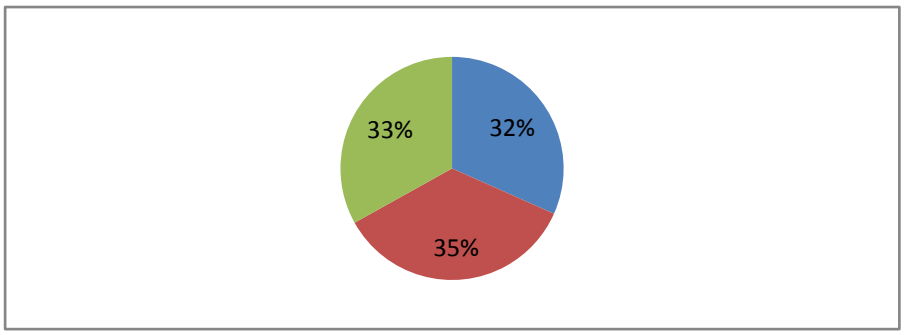

Figure (1): Culture results of 139 pregnant women included in the study.

Blood sampling:

With the use of syringes and needle, hand gloves and methylated spirit, cotton wool and tourniquet, some hematological values were measured from the blood sample of each subject was performed by withdrawing three mls of venous blood collected from the median cubital vein with minimum stasis, while subject was seated, and put it into sterile labeled tubes containing Ethylene di-amine tetra acetic acid (EDTA) acting as anti-coagulant, to Maternity Teaching Hospital laboratory where upon. Each was analyzed for full blood count including red blood cell(RBC), white blood cell (WBC) & platelet indices (RBC count, packed cell volume (PCV), hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red distribution width (RDW), WBC count, lymphocyte, monocyte, granulocyte, platelets (PLT) count, mean platelet volume (MPV) & plateletocrite (PCT). The results of the analyzed blood samples were generated by the analyzer, and displayed by a paper speed on thermal printing copy was performed using an automated hematology analyzer (Beckman coulter –ACT diff 1 &2, Germany) in the Maternity Teaching Hospital. Standardization, calibration of the instrument, and processing of the samples were done according to the manufacturer's instructions.

Statistical analysis:

The statistical analysis was done under the supervision of one well known statistician at Hawler Medical University. The Statistical Package for Social Sciences (SPSS) version 22 was used for data entry and analysis aided by Microsoft Excel 2013 to present the result in tables and figures. Data are expressed as mean ± slandered deviation (mean ± SD).

One- way analysis of variance (ANOVA) followed by Duncan's Post Hoc test was applied for multiple comparisons, and independent simple t-test Pearson's was applied for two different comparisons. A P value of <0.05 were considered as statistically significant.

Results:

In this study 243 subjects were included in this study, number, the frequency and the (Mean ± SD) of ages were calculated, the frequency of control group were 42.8%, while for the pregnant women according to the TMs

(1st, 2nd, 3rd) were (18.1%, 20.2%, 18.9%) respectively. The mean of age in control group was 32.41, and in cases were (27.14, 28.55, and 27.30) according to their TMs respectively. The minimum age was (16 and 19) years in control and case group while 46 year was the maximum age for both as shown in table (1).

Table (2) shows comparison between the different trimesters according to their groups. From 139 subject 15 were <20 years, 74 were between 20-29 years, 47 were between 30-39 year and 3 were between 40-49 years. In age < 20 year, 8(53.3%) were in the 1st trimester, 2(13.3%) were in the 2nd trimester, 5(33.3%) were in the 3rd trimester. Between 20-29 years, 23(31.1%) were in the 1st trimester, 24(32.4%) were in the 2nd trimester, 27(36.5%) were in the 3rd trimester. Between 30-39 years, 12(25.5%) were in the 1st trimester, 21(44.7%) were in the 2nd trimester, 14(29.8%) were in the 3rd trimester and between 40-49 years, 1(33.3%) were in the 1st trimester and 2(66.7%) were in the 2nd trimester. As total 44(31.7%) were in the 1st trimester, 49(35.3%) were in the 2nd trimester and 46(33.1%) were in the 3rd trimester. The statistical association was not significant between age groups and different trimesters.

Table (3) shows the hematological parameters of non- pregnant women (control) and pregnant women (cases). The mean values of the hematological parameters of RBC indices, such as RBC count, PCV and MCH shows a statistical significant difference between cases and control group in this study (P<0.001, 0.017 and 0.03 respectively).

Regarding WBC Indices, this study showed that there was a statistically significant difference in mean value of cases and control, in which mean of WBC count, percentage of Lymphocyte, Monocytes and Granulocytes were more in cases (pregnant women) than control group (non- pregnant women), P<0.001 for all. This study also revealed that the mean value of platelet count was less among pregnant women than non-pregnant women, (243.27 ± 60.02) versus (259.04 ± 57.37) and P=0.04.

The current study showed a statistically significant difference in Hb gm/dl between first and second trimester, in which it was lower in second trimester (11.69 ±1.18) versus (12.43 ± 1.38) in first trimester, p< 0.05. The percentage of lymphocyte was significantly less in second trimester (19.48 ± 6.83) versus (24.73± 6.40) in first trimester. This study also revealed that Plat. Count was significantly lower in third trimester (225.24±56.31) than second (241.96±58.87) and first (263.59±60.02), as shown in table (4).

Table (5) presents the comparison between the values of PCV, RBC count, WBC count & platelet count in control and case subjects at p-value < 0.05. Comparison between these parameters in our study as compare with other studies done in other parts of the world as shown in this table.

All studies reveal that there is highly significant difference in PCV, RBC count, WBC count & platelet count between healthy non pregnant women and healthy pregnant women and there is no more differences in results between our study and other studies done in other parts of the world, and all these changes around the normal physiological differences.

Table (1): Number, frequency and the (Mean + SD) of ages of the healthy pregnant and control (healthy non pregnant) groups.

Groups	No. (Frequency %)	Mean ± SD	Range
Control	104 (42.8)	32.41 ± 7.28	19 – 46
Case			
1st TM	44 (18.1)	27.14 ± 6.36	16 -42
2nd TM	49 (20.2)	28.55 ± 6.39	18 – 46
3rd TM	46 (18.9)	27.30 ± 5.44	17 – 39
Total	243 (100)	29.59 ± 6.69	16 – 46

Table (2): Comparison between the three trimesters according to their age groups.

Age	1st TM	2nd TM	3rd TM	Total	X^2/ Value
	No. (%)	*No. (%)*	*No. (%)*	*No. (%)*	
<20	8(53.3)	2(13.3)	5(33.3)	15(100.0)	
20-29	23(31.1)	24(32.4)	27(36.5)	74(100.0)	
30-39	12(25.5)	21(44.7)	14(29.8)	47(100.0)	
40-49	1(33.3)	2(66.7)	0(0.0)	3(100.0)	
Total	44 (31.7)	49 (35.3)	46 (33.1)	139 (100)	8.43/0.21

Table (3): Comparison of hematological parameters of Non-pregnant and Pregnant subjects.

Variables	Controls (104)	Cases(139)	p-value	Reference range
	Mean ± SD	*Mean ±SD*		
RBC Indices				
RBCc(10^6/uL)	4.54 ± 0.37	4.30 ± 0.41	<0.001	3.8 - 4.8
Hb (g/dl)	12.35 ± 1.14	12.05 ± 1.24	0.053	11.0 - 15.0
PCV (%)	38.83 ± 4.47	37.50 ± 4.13	0.017	36.0 - 46.0
MCV (fl)	85.57 ± 8.58	87.39 ± 8.31	0.1	76.0 - 96.0
MCH (pg	27.29 ± 2.54	28.05 ± 2.87	0.03	26.6 - 32.0
MCHC (g/dl)	31.94 ± 1.46	32.15 ± 2.03	0.343	31.5 - 37.0
RDW (%)	13.14 ± 2.43	13.46 ± 2.09	0.28	11.0 - 14.7
WBC Indices				
WBC c 10^3/uL	6.82 ± 1.71	9.01 ± 2.15	<0.001	4.0-11.0
Lymphocytes %	28.52 ± 7.24	21.17 ± 6.44	<0.001	20.5-51.1
Monocytes %	0.32 ± 0.13	0.53 ± 0.31	<0.001	1.7-9.3
Granulocytes %	4.37 ± 1.28	6.44 ± 1.78	<0.001	42.2-75.2
Platelet Indices				
PLT c 10^3/uL	259.04 ± 57.37	243.27 ± 60.02	0.04	150.0 - 450.0
MPV fl	8.04 ± 0.93	8.18 ± 1.09	0.293	7.8 - 11.0
PCT %	0.20 ± 0.047	0.20 ± 0.05	0.618	0.19 - 0.36

Table (4): Comparison of hematological parameters of pregnant women based on trimester.

Variables	1st TM (No.=44)	2nd TM (No.=49)	3rd TM (No.=46)
	Mean ± SD	*Mean ± SD*	*Mean ± SD*
RBC indices			
RBC count 10^6/ul	4.49 ± 0.39[a]	4.15 ± 0.43[b]	4.28 ± 0.37[b]
Hb gm/dl	12.43 ± 1.38[a]	11.69 ± 1.18[b]	12.08 ± 1.08[ab]
PCV %	39.27 ± 4.56[a]	35.92 ± 3.86[b]	37.50 ± 3.29[b]
MCV fl	87.61 ± 9.32[a]	86.68 ± 8.54a	87.95 ± 7.09[a]
MCH pg	27.76 ± 3.06[a]	28.05 ± 3.16[a]	28.35 ± 2.37[a]
MCHC g/dl	31.72 ± 1.61[a]	32.45 ± 2.64[a]	32.27 ± 1.57[a]
RDW %	12.93 ± 2.52[a]	13.81 ± 1.78[a]	13.62 ± 1.89[a]
WBC indices			
WBC count 10^3/ul	8.72 ± 2.23[a]	9.07 ± 2.13[a]	9.25 ± 2.13[a]
Lymphocytes %	24.73 ± 6.40[a]	19.48 ± 6.83[b]	19.59 ± 4.50[b]
Monocytes %	0.52 ± 0.32[a]	0.56 ± 0.38[a]	0.51 ± 0.23[a]
Granulocytes %	5.93 ± 1.82[a]	6.60 ± 1.75[ab]	6.76 ± 1.72[b]
Platelets indices			
Plat. count 10^3/ul	263.59 ± 60.02[a]	241.96 ± 58.87[ab]	225.24 ± 56.31[b]
MPV fl	8.16 ± 1.42[a]	8.32 ± 0.98[a]	8.06 ± 0.85[a]
PCT %	0.22 ± 0.07[a]	0.19 ± 0.05a[b]	0.19 ± 0.045[b]

The different letters mean there is statistically significant difference between groups, P<0.05.

Table (5): comparison of the results of our study with other studies.

		This study	Abia State	Bankura	Benin State	North Nigeria
PCV	*Control*	38.83± 4.47	39.20 ± 1.60	37.73± 3.69	37.60± 0.70	39.73±4.68
	Case	37.50± 4.13	34.10 ± 2.40	30.68± 4.26	32.60± 0.97	36.00±2.60
	P- value	< 0.05	< 0.05	< 0.05	< 0.01	< 0.001
RBC	*Control*	4.54± 0.37	5.20 ± 2.20			4.60 ± 0.61
	Case	4.30 ±0.42	3.45 ± 1.70			4.27 ± 0.45
	P- value	< 0.001	< 0.05			< 0.001
WBC	*Control*	6.82 ± 1.71	4.20 ± 1.40	4.91 ± 0.88	5.05 ± 0.34	4.61 ± 1.05
	Case	9.01 ±2.15	6.10 ± 2.70	7.26 ± 3.02	6.62 ± 0.51	6.62 ± 1.50
	P- value	< 0.001	< 0.05	< 0.05	< 0.05	< 0.001
Platelet	*Control*	259.04±57.37	198.50± 5.60		255.40± 24.	240.95±59.65
	Case	243.27±60.02	122.00± 3.40		184.22±12.24	215.44± 58.4
	P- value	< 0.05	< 0.05		< 0.05	< 0.01

Discussion:

This present study was to compare hematological indices of pregnant (cases) and non-pregnant (control) women and also to evaluate the hematological parameters of pregnant women at different trimesters (first, second and third). As it shows in the result that there is a significant difference in the RBC counts, PCV and MCH between the pregnant and non-pregnant.

Hematological profile is measured all over the world to estimate general health, because it is a reliable indicator and is a simple, fast and cost-effective test [(12)]. In addition, the hematological

profile is considered to be one of the factors affecting pregnancy and its outcome [13].

Physiological changes occur during pregnancy and can be observed in hematological indices such as RBC count, Hb concentration, PLT count, and WBC count. Some of these are decreased - for example, RBC and PLT counts - partly as a result of the physiological hemodilution that occurs in pregnancy, [14] while others are increased, such as the WBC count [15]. Unfortunately we didn't find any studies about hematological profile n healthy pregnant and non pregnant women done inside the Iraq apart the studies done on anemia in pregnant women.

This study showed significant drop in red blood cells in general in pregnant women when compared with non – pregnant also significant change when compared between first and second trimester and increased in the third trimester and this may be due to increases in plasma volume about (25%–80%) between the sixth and twenty-fourth week of gestation.[16] However, the increase in RBC count has been found to be approximately (30%) between the twelfth and thirty-sixth week of gestation when iron and folate are supplemented [17]. The discrepancy between the rate of increase in plasma volume and that in RBC mass leads to physiological anemia.

The result of this study agreed with the study done by Michael& Nazli [18]which showed that RBC count begins to increase at 8–10 weeks of gestation and steadily risen by (20–30%) (250–450 mL) above non-pregnant levels by the end of pregnancy in women receiving iron supplementation [19]. Among women not on iron supplements, the RBC count may only increase by (15–20%) [20]. Erythrocyte life span is slightly decreased during normal pregnancy and Erythropoietin levels increase by (50%) in normal pregnancies and vary according to the presence of pregnancy complications [21]. The increased plasma erythropoietin induces the rise in RBC count, which partially supports the higher metabolic requirement for oxygen during pregnancy [22].

This study showed significant drop in Hb in general in pregnant women when compared with non - pregnant while significant change when compared between 1st and 2nd trimester and increased in the third trimester and this may be due to the progressive decline in Hb concentration from the 1st to 2nd trimester may be due to an increased demand for iron as pregnancy progresses and more iron is required to meet the needs of fetal growth. The additional progesterone and estrogen that are secreted by the placenta during pregnancy cause a release of renin from the kidneys. Renin stimulates the aldosterone-renin-angiotensin mechanism, leading to sodium retention and increased plasma volume. The increase in plasma volume is relatively greater than the increase in RBC count, which results in a fall in maternal Hb, hence the physiological anemia occurs in pregnancy [3].

In this study the MCV increased in pregnant women (cases) when compared to the non-pregnant (control) with in the first trimester and declined in the second trimester and increased in the third trimester and this agreed with a study done by (Surabhi*etal*) who stated that there is a small increase in MCV, of an average of 4 fl in an iron-replete woman, which reaches a maximum at 30–35 weeks gestation and does not suggest

any deficiency of vitamins B12 and folate. Increased production of RBCs to meet the demands of pregnancy, reasonably explains why there is an increased MCV (due to a higher proportion of young RBCs which are larger in size) [(1)].

In our study there was increasing in white blood count in pregnant women in comparison to the non –pregnant women and the trimester distribution of leucocyte counts in this study shows a progressive increase with gestational age although it is statistically not significant between the first, second and the third trimesters is a pointer to the concept of a boost in leucocyte function in pregnancy. This is consistent with the results of many other studies in Nigeria [(3)].

In pregnancy, humoral immunity is said to be intact, but cell mediated immunity is markedly depressed, up regulation of innate immunity has been theorised to be a compensatory mechanism [(23)].

leukocytosis which is due to physiological stress occur early in pregnancy and remain elevated throughout pregnancy [(24)]. There WBC count during healthy pregnancy vary from 6×10^9-16×10^9/L which further increases to 9×10^9-25×10^9/L hours after delivery [(25)]. It takes 4 weeks time for WBC count to come back to normal after delivery [(26)].

The white blood cells (leucocytes) are the cellular components of blood mediating the body's immune system. They constitute about (1%) of blood cells. Leucocytes originate form pluripotent stem cells in the bone marrow. There are five subsets; neutrophils, eosinophils, basophils, lymphocytes, and monocytes [(27)]. Pregnancy is associated with alterations in many haematological parameters, one of which is an increase in white blood cell count (leucocytosis). It has been attributed to physiologic stress and increased inflammatory response associated with pregnancy [(28)]. This leucocytosis is mainly due to neutrophilia and immature forms like metamyelocytes and myelocytes (neutrophil left shift) may be present in the peripheral blood film. Monocytosis is also reported in pregnancy [(29)].

A major change in innate immunity noted is an increase in WBC count mainly due to neutrophilia, several changes have been reported in neutrophils during pregnancy. They include; impairment of apoptosis due to the increased inflammatory response reduced chemotaxis and impaired respiratory burst [(30)].

Crocker *et al* [(31)] observed that peripheral blood neutrophils in normal pregnancy were neither primed nor activated, but their release of reactive oxygen species (ROS) was impaired. Thus, the neutrophilia of pregnancy is associated with a left shift to enhance phagocytosis by engaging younger band forms and there may be toxic granulations due to poor oxidative metabolism [(32)].

This boost in non-specific (innate) immunity is said to be a compensation for the attenuation of specific immunity in pregnancy, the impairment of specific immunity correlates with a reduction in lymphocyte count in pregnancy [(33)].

In this study there was a decrease in the lymphocyte count in pregnant women(cases) in comparisons with non-pregnant(controls) and continue to decrease in the second and third trimester and this agreed with (Surabhi *etal*) who stated that lymphocyte count decreases during pregnancy through the

first and second trimesters and increases during the third trimester [1].

There is a monocytosis during pregnancy, especially in the first trimester, but decreases as gestation advances. Monocytes help in preventing fetal allograft rejection by infiltrating the decidual tissue (7^{th}-20th week of gestation) possibly, through prostaglandin E2 (PGE2) mediated immunosuppression [34].

In this study showed that platelet was significantly lower in pregnant women in comparison with the non –pregnant women and the platelets counts continued to decrease in the second and third trimester and this agreed with a study done by (Obeagu*etal*) who record the same finding [5].

The PLT count is slightly lower in pregnant than in non-pregnant women and most studies report an approximate (10%) lower PLT level at term compared with PLT counts at pre-pregnancy [35].

After anemia, thrombocytopenia is the second most common hematologic abnormality that occurs during pregnancy [36].

Gradual reduction in PLT count as pregnancy advanced due to hemodilution secondary to expansion of plasma volume, increased platelet aggregation driven by increased level of thromboxane A_2, the PLT count in normal pregnancies may decrease by approximately (10%), with most of this decrease occurring during the third trimester although the PLT count tends to remain within the normal reference range in most patients [37]. However, Van Buul *etal* reported an increase in PLT count in pregnancy [38].

Most cases of thrombocytopenia in pregnancy are mild, with no adverse outcome for mother or baby, occasionally a low PLT count may be part of a complex disorder with significant morbidity and be (rarely) life-threatening [39].

Overall, about (75%) of cases of PLT changes are due to gestational thrombocytopenia, (15%-20%) secondary tohypertensive disorders, (3%-4%) due to an immune process, and the remaining (1%-2%) comprises rare constitutional thrombocytopenias, infections, and malignancies [40].

Conclusions:

1. Pregnancy is one of the factors affecting the hematological parameters and it's consider as physiological change that is occur in healthy pregnant women in comparison with non-pregnant.
2. Significant differences were observed in RBC count, PCV, Hb between three TMs.
3. WBC count was increased non-significantly, while lymphocyte and granulocyte were increased significantly.
4. Platelet count and platletocriate significantly decreased among TMs.

Recommendations:

1. We recommended to follow up every pregnant woman within different TMs and do a blood examination to them as a normal routine investigation to detect and differentiate either its physiological or pathological changes.
2. Every medical staff in antenatal care center should have an idea about normal physiological changes in blood indices.
3. Prophylactic iron supplement have to be given to all pregnant women to avoid anemia.

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