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Obstetrical Aspect of Iron Deficiency Anemia in Iraqi Patients

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Abstract. *Background .Iron deficiency anemia is the most frequent type of anemia during pregnancy*
Aim of the study .To evaluate the prevalence of iron deficiency anemia in Iraqi patients and to correlate the findings with the obstetrical aspects
Method .This study including 50 pregnantIraqi females from all three trimester of pregnancy .data was obtain during the first and second and third trimester also including as well as previous medical obstetrical history
Result. 62% of female patient have iron deficiency anemia in the third trimester, and 46% of them were above 30 year old
Conclusion .iron deficiency anemia mostly affected female more than 30 years old especially in the third trimester with ahistory of 1-2 year interpregnancy interval
Keywords .*anemia obs Iraq patient*

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I. Introduction

Anemia is defined as the reduction in absolute number of the circulating red blood cell (RBC) indirectly measured by reduction in hemoglobin(Hb) concentration ,hematocrit (Hct)or RBC count (Breymann C et.al, 2010,ribot B et.al , 2012,pena Rosas Jpet. Al, 2012 and Ana Gomesda,et.al ,2016).

In 2014 the world health organization (WHO),has defined anemia as Hb less than 11.gm/dl in the first trimester,less than 10.5gm/dl in the second trimester and less than 11gm/dl in the third trimester (De benoist B , et. al ,2008,Berger J .et,al 2011,Goon ewardene M. et. al 2012, and WHO/NHD/2014).

Furthermore iron deficiency anemia (IDA) affect many people world wide and consequently female at reproductive age and pregnant women (Hess SY .et,al 2001 and Noronha. JA 2014).

Ironically multiple contributing factors may lead to (IDA) during pregnancy .reduced iron intake ,eating disorder ,blood loss ,defect in the iron metabolism (UNICEF/uno/WHO 2001,Candio F .et,al 2007 and MIman N.et,al 2008).Other factors with less affect may lead to the above complication ,(hemolysis and abnormal hemoglobin synthesis with mostly associated with agenetic disorder)(ACOG,2008 and Scholl TO .et,al 2011).

Hediger,ML.et,al, 1992 and Scholl ,TO et,al 2011 assumed that the risk factor mostly related to (IDA) .multiple gestation ,high parity , frequent pregnancies and reduced interpregnancy interval ,also they consider that teenage pregnancies and extremes of maternal age and smoking also may lead to (IDA)

Traditionally several clinical problem may associated with anemia like infection , higher risk of postpartum anemia ,increase of the frequency of preterm delivery ,depression ,chronic placental insufficiency ,low birth weight and small for the gestational age infant (Murphy JF 1986 ,Leieberman E et,al.1988 , LUZM 1991,Klebanoff MA.et,al 1991 and Giancarlo.et,al2015).

Clinical studies assessing the highest risk of anemia and poor physical and mental growth during infancy and the risk of sever maternal morbidity or mortality after post partum hemorrhages mostly co exsit with (IDA)(Debenoist.B et,al 2008,Breymann c 2010.et,al ,Milman N.et,al ,2012and Ana Gomesda.et,al 2016).

There are many studies that support the role of the nutritional deficiency in (IDA)(Chandra S et,al, 2012)However ,this may due to the fact that diet in pregnancy is insuffient to supply the iron requirement (WHO/MCH/MSM/1992).

Other reserchers confirm that during pregnancy there is a physiological hemodilution reaching a peak 20-24 weeks of gestation with a physiological drop due to higher increase in plasma volume ,compared with red blood cell mass which slightly increase during pregnancy (Rahman MM.et,al, 2016 and RimpyTandon.et,al 2018).

This physiological process produces relative hemodilution blood viscosity ,helping the blood circulation in the placenta (Soltzfus.et,al1998 , Chandra S.et,al 2012 ,Pena-Rosas JP dene M,2012 and Goon.eward 2012).

Thereis agreat contributing related to the role of the iron transfer to the fetus occurs during the second and the third trimester (Both Well TH 2000,and RammohanAetal 2012).

Other researches still discuss that the rapid growth of the fetus occurs in the third trimester so the iron and micronutrient demandsare highest in the this trimester (Rusia.et,al 1995,and Allen. LH 2000).Several studies covering different aspects of (IDA) including the prevalence ,epidemiological, ethnic, and different trimester period ,up to our knowledge this is the first study which cover these aspect with details in Iraqi pregnant patients including the effect of the different trimester.

II. Aims of the study

This study was conducted to

1.Evaluate the prevalence of the of iron deficiency anemia in Iraqipregnant female.

2.Correlate the findings with the age of the pregnant female ,gestational age ,interpregnancy interval,parity,history of the abortion ,history of bleeding during pregnancy and associated disease during pregnancy.

III. Materials and methods

Subjects

The study population including pregnant Iraqi female, they visited the antenatal care clinic in Baghdad (January 2016 to march2018). Informed consent was signed for the ethical approval (appendix1).

All pregnant women attending their first clinic visit for antenatal care at 8 week or less wereinvited to participated in this study The diagnosis of (IDA)was confirmed according to the criteria of the center of the disease control (Beutler. E et,al 2006.WHO 2011 ,VMNISandStevans.GA ,2013).which defines anemia as HB less than 11gm/dl (hematocrit less than 33%) in the first trimester ,Hb less than 10.5 gm/dl(hematocrit less than 32%) in the second trimester and less than 11gm/dl(hematocrit less than 33%) in the third trimester(Daru J.et,al 2016).

Previous medical and obstetrical history included maternal age ,parity ,gestational age ,multifetal pregnancies association disease ,and interpregnancy intervals.

Exclusion criteria including patients currently on iron treatment ,history of hematological disease ,blood transfusion in the previous 6 months ,chronic inflammation ,endocrine diseases ,patient with history of blood loss and history of autosomal dominant or recessive blood disease

IV. Materials

Equipment and instruments used in hematological process

- Test tube
- OLymic microscope
- Racks
- Tournica
- Clean glass slide
- Automatic hematology analyzer
- Glass marking pencil
- Centrifuges
- Sterile goaze pads
- Autoclaves
- Screw cappet bottle
- Tweezers
- Micropipette with different size
- Solution and chemicals
- Giemsa stain
- EDTA
- Potassium cyanide
- Oil emersion for the microscope

V. Methods

Three to four ml of blood was drawn from each individual at morning between (8-10) a.m ,from vein of the arm ,using heparinized syringe washed with heparin and transported to the laboratory in cool box for the hematological study this method was done by the followings:

Clean the skin with antiseptic wipe ,place the tourniquet around the upper arm then inserted a needle in the arm and collect blood sample in one or more vial .remove the tourniquet .then cover the area with a bandage to stop any bleeding.

Label the sample and send to the lab by the cool box to perform the followings test ;Hb concentration ,ferritin, MCV.MCH,MCHC,pcv,and complete blood film Each one of the patients who came for the first antenatal visit was screened for anemia This study including pregnant females from all three trimester of pregnancy .data was obtain during the first and second and third trimester also including as well as previous medical and obstetrical history

Statistical Analysis[(1)] :

The following statistical data analysis approaches were used in order to analyze and assess the results of the study under application of the statistical package (SPSS) ver. (22.0) :

1. Descriptive data analysis:

a- Tables (Frequencies, and Percentages), as well as mean and standard deviation.
b- Contingency Coefficients for the association tables.
c- Graphical presentation by using :
- Cluster Bar Charts.
- ROC curve Charts

2. Inferential data analysis:

These were used to accept or reject the statistical hypotheses, which included the following :

a- Contingency Coefficients (C.C.) test for the cause's correlation ship of the association tables.

$$C.C. = \sqrt{\frac{\chi^2}{\chi^2 + T..}}$$

Where χ^2 is the Chi Square statistic and T.. is the overall total of the contingency table.

b- Binomial test for testing the different of distribution of the observed frequencies of two categories nominal /or ordinal scale and there is none restricted of an expected outcomes at 50%.

The binomial probability, b(x; n, p), is calculated using:

$$b = \underset{x}{n} C p^x q^{n-x}$$

c- Screening tests: Tests for mining data and estimating several indicators, such that (Sensitivity Rate, Specificity Rate).
d- Receiver Operation Characteristic curve [ROC] curve and estimating Area, as well as estimating 95% confidence interval, with standard error, asymptotic significant level Receiver Operation Characteristic [ROC] curve.
e- Contingency coefficient test is a measure of association ranges between zero and 1, with zero indicating no association between the row and column variables and values close to 1 indicating a high degree of association between the variables. The maximum value possible depends on the number of rows and columns in a table
f- McNemar test: A nonparametric test for two related dichotomous variables.Tests for changes in responses using the chi-square distribution. Useful for detecting changes in responses due to experimental intervention in "before-and-after" designs. Typically, a significance value less than 0.05 is considered significant.

For the abbreviations of the comparison significant (C.S.), we used the followings:

- NS : Non significant at P>0.05
- S : Significant at P<0.05
- HS : Highly significant at P<0.01

(1) All the Statistical Analysis and Findings results were Supervised by Bio-Statistician Prof. (Dr.) Abdulkhaliq Al-Naqeeb, College of Health and Medical Technology, Baghdad – Iraq.

VI. Results and Findings

This chapter presents the findings of data analysis systematically in tables and these correspond with the objectives of this study, and as follows:

I. Descriptive of studied Parameters:

Table (1-1) represented distribution of reproductive parameters, as well as comparisons significant comparing observed frequencies' distribution in contrast of an expected outcomes under a similarity distributionamong differentgroupsin each variable whether they having the same proportion or not.

Table (1-1): Distribution of reproductive parameters with comparisons significant

Reproductive variables	Groups	No.	%	C.S.
Age Groups	15 _ 19	8	16	χ^2= 7.120 P=0.212 (NS)
	20 _ 24	8	16	
	25 _ 29	11	22	
	30 _ 34	13	26	
	35 _ 39	7	14	
	40 _ 44	3	6	
	Total	50	100	
	Mean ± SD	28.32 ± 7.01		
No. of Gravida	1 _ 2	21	42	χ^2= 8.440 P=0.015 (S)
	3 _ 4	22	44	
	5 _ 6	7	14	
	Total	50	100	
No. of Parity	Non Applicable	13	(26)	P=0.021 (S)
	1 _ 2	26	70.3	
	3 _ 4	11	29.7	
	Total	50	100	
No. of Gravida to No. of Parity Groups	Non Applicable	13	(26)	P=0.511 (NS)
	< 2	21	56.8	
	2 _ 3	16	43.2	
	Total	50	100	
No. of Abortion	Absent	38	76	P=0.000 (HS)
	Present	12	24	
	Total	50	100	
Anemia in gestational age Trimester 1st	Neg.	37	74	P=0.001 (HS)
	Pos.	13	26	
	Total	50	100	
Anemia in gestational age Trimester 2nd	Neg.	25	50	P=1.000 (NS)
	Pos.	25	50	
	Total	50	100	

Continue …

Reproductive variables	Groups	No.	%	C.S.
Anemia in gestational age Trimester 3rd	Neg.	19	38	P=0.120 (NS)
	Pos.	31	62	
	Total	50	100	
Gestational No.	Non applicable	4	(8)	P=0.000 (HS)
	One	44	95.7	
	Two	2	4.3	
	Total	50	100	
Inter pregnancy interval	Non applicable	13	(26)	χ^2= 11.600 P=0.009 (HS)
	1 _ 2	21	56.8	
	3 _ 4	12	32.4	
	5 and more	4	10.8	
	Total	50	100	
Association disseat during pregnancy	Neg.	47	94	P=0.000 (HS)
	Pos.	3	6	
	Total	50	100	
Hx of bleeding during pregnancy	Neg.	44	88	P=0.000 (HS)
	Pos.	6	12	
	Total	50	100	
Iron supplementation	Neg.	50	100	P=0.000 (HS)
	Pos.	0	0	
	Total	50	100	

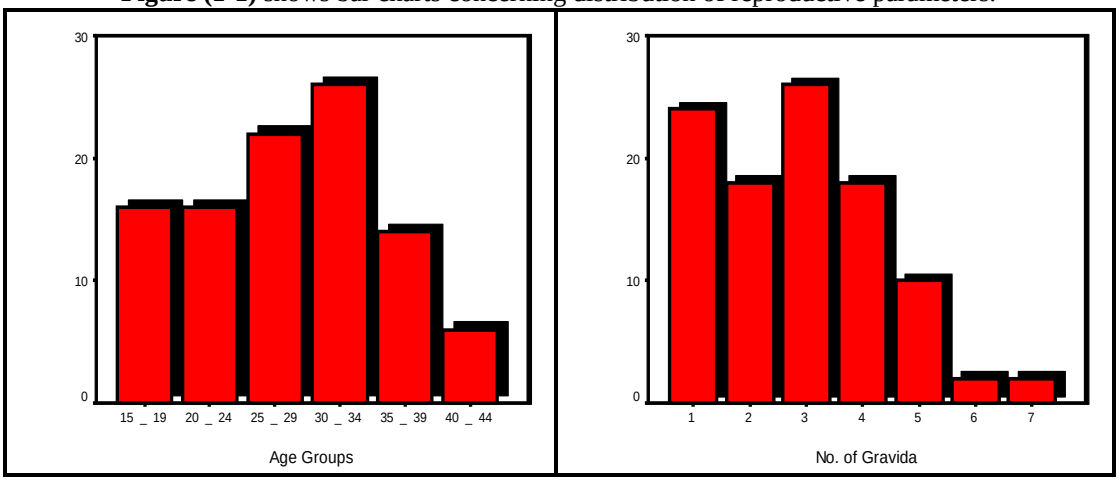
(*) HS: Highly Sig. at P<0.01; S: Sig. at P<0.05; NS: Non Sig. at P>0.05;Testing based on One-Sample Chi-Square test, and the Binomial test.

Results shows that age groups seems to be having bell shape distribution, with mean and standard deviation values 28.32 yrs., and 7.01 yrs. respectively, as well as no significant at P>0.05 are accounted among different age groups compared with an expected distribution.Most numbers of Gravida are recorded in the first and second groups, as well as significant different at P<0.05 are accounted among different numbers of Gravida groups compared with an expected distribution.Most numbers of Parities are recorded in the first group, as well as significant different at P<0.05 are accounted among different numbers of Parities groups compared with an expected distribution.Likeness numbers of Gravida to Parities ratio are recorded in the first and second groups statistically, since no significant different at P>0.05 are accounted among different groups compared with an expected distribution.

Rather than most numbers of studied individuals who had no abortion, but a positive numbers state accounted for large proportion indeed, since they recorded 12(24%), as well as highly significant different at P<0.01 are reported between numbers for who had abortion or not.Rather than most numbers of studied individuals who hadn't anemia in gestational age trimester 1st, but a positive numbers state accounted for large proportion, since they recorded 13(26%), as well as highly significant different at P<0.01 are reported between numbers who had positive numbers or not.A similar numbers of studied women in gestational age trimester 2nd who had, and hadn't anemia was reported, and they recorded 25(50%), as well as no significant different at P>0.05 are reported.Rather than most numbers of studied individuals who had anemia in gestational age trimester 3rd, and has recorded 31(62%), as well as highly significant different at P<0.01 are reported between numbers for who had positive numbers or not.Most gestational numbers has assigned only one, and has recorded 44(95.7%), as well as highly significant different at P<0.01 are accounted.

Most numbers of inter pregnancy interval are recorded in the first group, and has recorded 21(56.8%), as well as highly significant different at P<0.01 are accounted.
Most numbers of association disseat during pregnancy are recorded negativestate, and has recorded 47(94.0%) with highly significant different at P<0.01.
Most numbers of Hx of bleeding during pregnancy are recorded negative state, and has accounted 44(88.0%) with highly significant different at P<0.01.
Finally, all numbers of Iron supplementation are recorded negative state, and has accounted 50(100%) with highly significant different at P<0.01.

Figure (1-1) shows bar charts concerning distribution of reproductive parameters.



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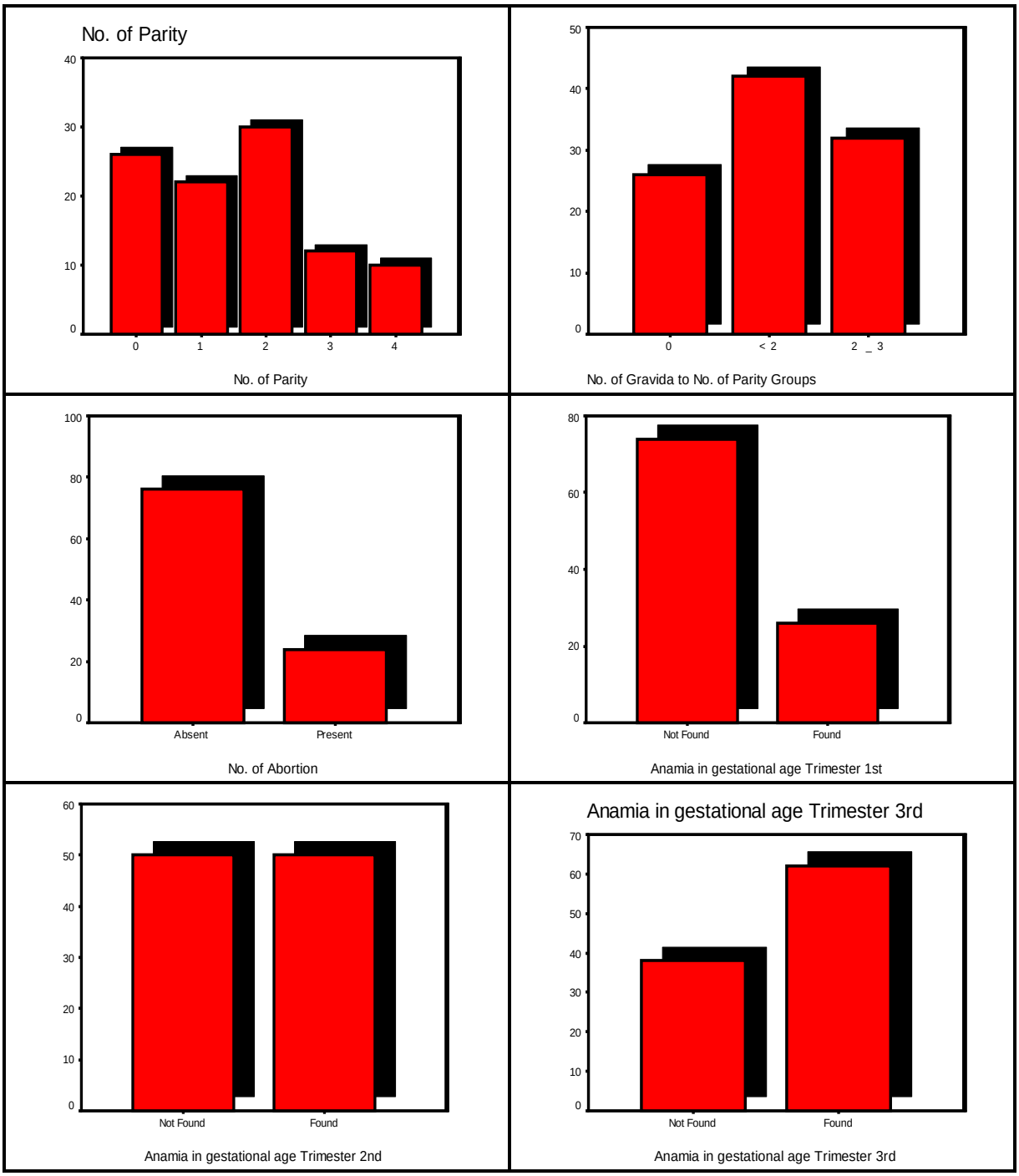
No. of Parity
40
30
20
10
0
0
1
2
3
4
No. of Parity
50
40
30
20
10
0
0
< 2
2 _ 3
No. of Gravida to No. of Parity Groups
100
80
60
40
20
0
Absent
Present
No. of Abortion
80
60
40
20
0
Not Found
Found
Anamia in gestational age Trimester 1st
60
50
40
30
20
10
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Not Found
Found
Anamia in gestational age Trimester 2nd
Anamia in gestational age Trimester 3rd
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Anamia in gestational age Trimester 3rd

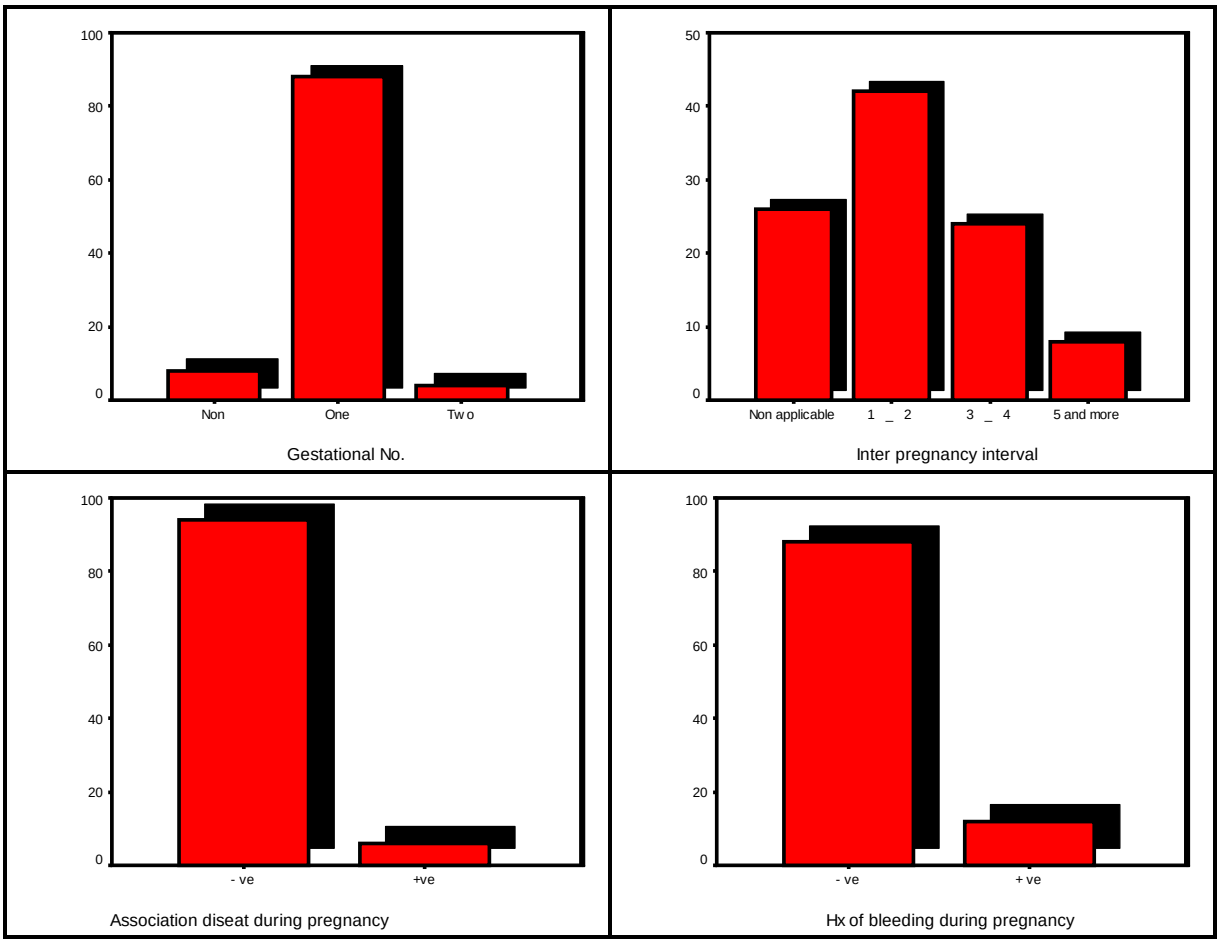


Figure (4-1-1): Bar Charts plotsforDistribution of Reproductive Parametersof theStudied Sample

Table (1-2) shows distribution observed frequencies (Pos., and Neg.) outcomes in light of testing (Repeated measurement)sequentially, with comparison.

Table(1-2): Distribution of Anemia in Gestational Age Trimesters Sequentially with comparisons significant

(1st X 2nd)			2nd Pos.	2nd Neg.	C.S. (*)
1st	Pos.	No.	1	12	P=0.065 NS
		1st %	7.7%	92.3%	
		2nd %	4.0%	48.0%	
	Neg.	No.	24	13	
		1st %	64.9%	35.1%	
		2nd %	96.0%	52.0%	
(2nd X 3rd)			**3rd Pos.**	**3rd Neg.**	
2nd	Pos.	No.	11	14	P=0.392 NS
		2nd %	44.0%	56.0%	
		3rd %	35.5%	73.7%	
	Neg.	No.	20	5	
		2nd %	80.0%	20.0%	
		3rd %	64.5%	26.3%	
(1st X 3rd)			**3rd Pos.**	**3rd Neg.**	
1st	Pos.	No.	8	5	P=0.001 HS
		1st %	61.5%	38.5%	
		3rd %	25.8%	26.3%	
	Neg.	No.	23	14	
		1st %	62.2%	37.8%	
		3rd %	74.2%	73.7%	

(*) HS: Highly Sig. at P<0.01; NS: Non Sig. at P>0.05;Testing based on McNemar test.

Results shows that, (Repeated measurement)sequential test between (1^{st} X 2^{nd}) trimesters, and rather than no significant different at P>0.05 which was assigned, but the real (P_{-value} =0.065) which enable to says that it's more informative for that result to be reported rather than simply stating that significant level was not achieved, Robert 2006.and according to that, about half of studied women were suffering from anemia when they achieved to the second trimesters.

In addition to that, sequential test between (2^{nd} X3^{rd}) trimesters are accounted no significant different at P>0.05, although anemia remains high by the age of gestation. finally, results shows that, (Repeated measurement)sequential test between (1^{st} X 3rd) trimesters represented highly significant different at P<0.01, which enable to says that it's more informative for that result to be reported, and accordance to that, about half of studied women were suffering from anemia when they achieved to the third trimesters.

Table (2-2) show estimation area of trade - off between sensitivity and specificity through plotting sensitivity against specificity to examine that trade - off, which is called a receiver operating characteristic or ROC curve, as well as significant level for testing area parameter under fifty percent, with 95% confidence interval of area parameter.

Table (2-2): ROC Curve of Anemia in Gestational Age follow up Sequentiallyregarding different Trimesters

Trimesters	Sensitivity	Specificity	Area	Std. Error	Asymp. Sig.	Asymptotic 95% C.I.	
						L.b.	U.b.
1st X 2nd	0.923	0. 649	0.786	0.068	0.002	0.652	0.919
2nd X 3rd	0.560	0.800	0.680	0.077	0.029	0.529	0.831
1st X 3rd	0.385	0.622	0.503	0.094	0.974	0.319	0.687

(*)Non Sig. at P>0.05; The positive actual state is Positive.

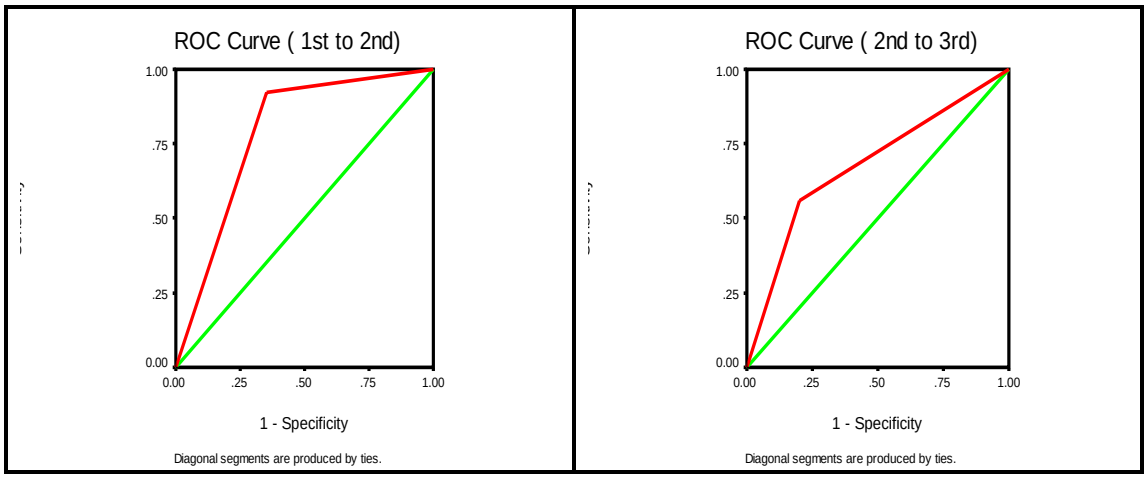
Results shows that contrast between (1^{st}X 2^{nd}) trimesters, has recorded highly significant area which was represented by ROC curve at P<0.01, and accordance with that result it could be indicating that anemiamarker with studied women reported low level indicator for women's diagnosis among those who has in the 1^{st} trimester and 2^{nd} trimesters.

In addition to that, screening tests concerning sensitivity, specificity, and area under ROC curvewith reference to anemia marker in light sequential test between (2^{nd} X 3^{rd}) trimesters gave a meaningful indicator in the second order, since significant different are accounted at P<0.05.

Finally, results shows that contrast between (1^{st}X 3^{rd}) trimesters, has recorded no significant area (Area = 0.503), which was represented by ROC curve at P>0.05, and accordance with that result it could be indicating that anemiamarker with studied women reported high level indicator for women's diagnosis among those who has in the 1^{st} trimester and 3^{rd} trimesters.

It could be conclude that the third anemia contrast between (1^{st}X 3^{rd}) trimesters was overrated of morbidity compared with the others contrasts of trimesters, rather than stating that three contrasts are reliable for studying anemia as good indicator for studied pregnant women along passing the age of gestation in descending way.

Figure (2-1) show ROC curve concerninganemia markerresponding according to compare (1^{st} X 2^{nd}, and 2^{nd} X 3^{rd}) trimesterperiods.



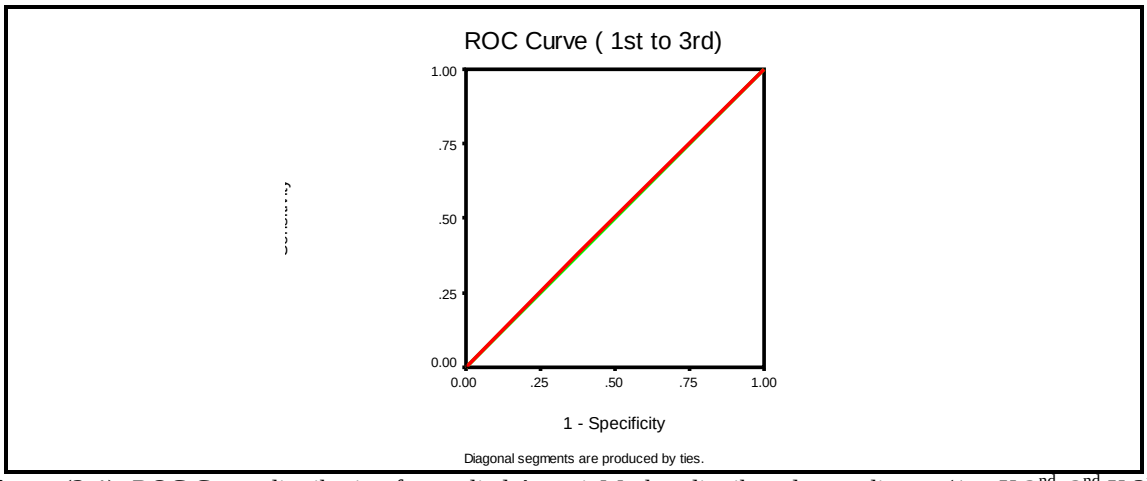


Figure (2-1): ROC Curve distribution for studied AnemiaMarker distributed according to (1st X 2nd, 2nd X 3rd, and 1st X 3rd) trimesters periods

To find out relationships between Hx of bleeding during pregnancy (BDP) and studied reproductive parameters, table (2-3) shows contingencies coefficients with their significant levels under the null statistical hypothesis which says that a meaningless relationships are occurred between preceding parameters in light of (BDP) marker, and results illustrated no significant relationships at P<0.05 are accounted indeed.

Table (2-3): Relationships between Hx of Bleeding During Pregnancy (BDP) and studied Reproductive Parameters

Parameters		C.C.	P-value(*)
Age Groups		0.311	0.376
No. of Gravida		0.346	0.339
No. of Parity		0.184	0.730
No. of Gravida to No. of Parity		0.218	0.175
No. of Abortion		0.219	0.112
Anemia in Gestational Age	Trimester 1st	0.198	0.153
	Trimester 2nd	0.122	0.384
	Trimester 3rd	0.160	0.251
Inter Pregnancy Interval		0.144	0.788
Gestational No.		0.228	0.133

(*)Non Sig. at P>0.05

To find out related ratios between Hx of bleeding during pregnancy (BDP) and studied reproductive parameters, table (2-4) shows an odds ratio coefficients with their 95% confidence intervals, which indicating that a meaningless related ratios are occurred between preceding some of reproductive parameters in light of (BDP) marker.

Table (2-4): Related Ratios (Odds Ratio) of (BDP) marker and studied Reproductive Parameters

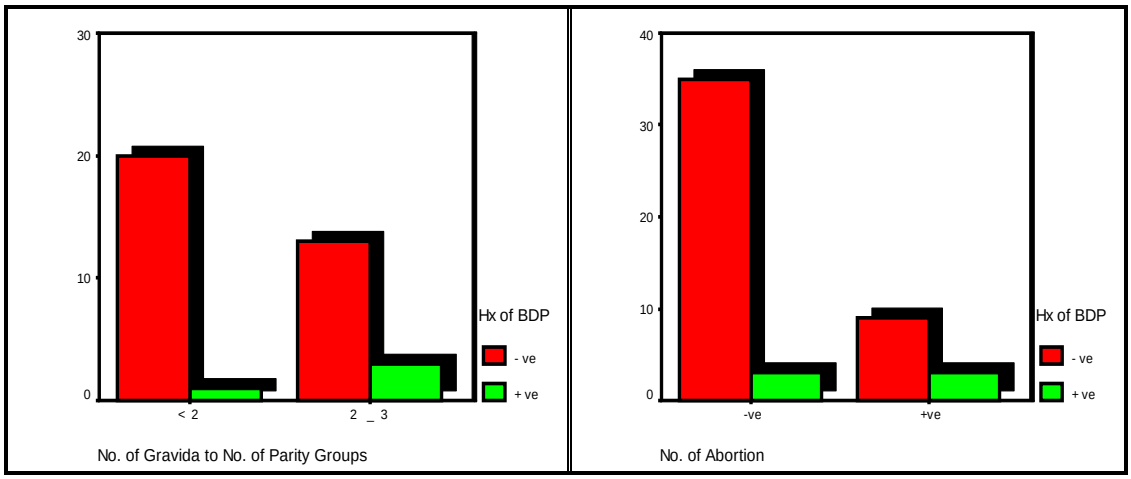
Parameters		Odds Ratio	95% Confidence Interval	
			Lower	Upper
No. of Gravida to No. of Parity		4.615	0.432	49.296
No. of Abortion		3.889	0.669	22.604
Anemia in Gestational Age	Trimester 1st	3.400	0.592	19.541
	Trimester 2nd	0.457	0.076	2.755
	Trimester 3rd	3.462	0.372	32.178
Gestational No.		7.800	0.419	145.200

(*)Non Sig. at P>0.05

Regarding Pos. of one case concerning (BDP) marker of < 2 ratio of (No. of Gravida to No. of Parity) group is a contrast for five pos. cases approximately (1 : 4.615), within the effectiveness of neg. proportion betweenthe two ratios groups.

Concerning Pos. of one case concerning (BDP) marker of (No. of Abortion) is a contrast for four pos. cases approximately (1 : 3.889) within effectiveness of neg. proportion betweentwo ratios groups. Anemia in gestational age regarding 1st and 3rdconcerning (BDP) marker, area contrast for pos. cases are approximately (1 :3.41).

Finally, on the subject of Pos. of one case concerning (BDP) marker is a contrast for eight pos. cases approximately (1 :7.8), within the effectiveness of neg. proportion betweenthe two ratios groups.
Figure (2-2) show cluster bar chartsconcerning(BDP) markerdistributed according to studied reproductive parameters.



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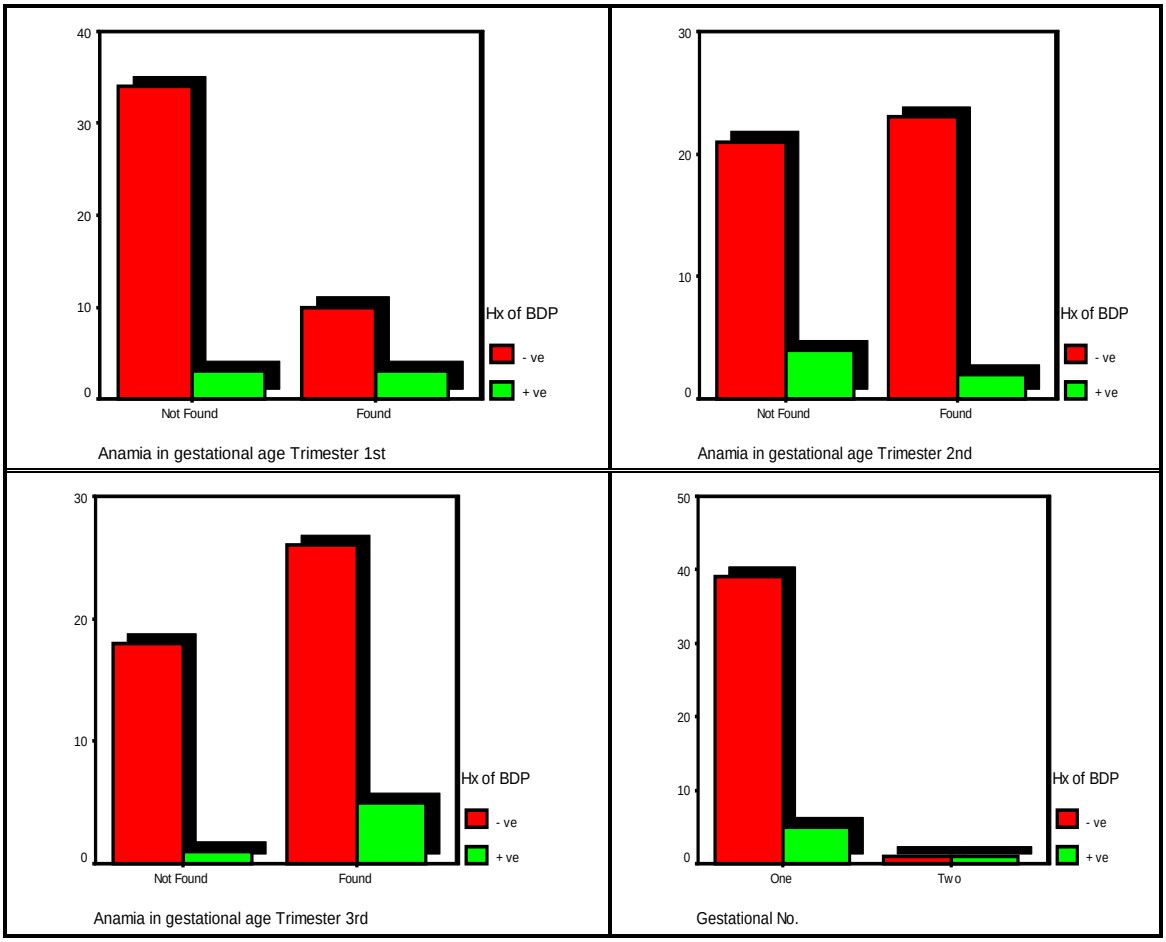

Figure (2-2): Cluster Bar Charts concerning (BDP) markerdistributed according to studied reproductive parameters

VII. Discussion

The most common type of anemia in pregnancy is iron deficiency anemia. That cause many problem for both mother and fetus like a small for gestational age infants ,poor physical and mental growth during infancy, highest risk of anemia ,increased susceptibility to maternal infection and higher risk of post-partum depression (Lee A.e,tal 2011 and Christain and Breymam MD .et,al 2015).

This study showed that the prevalence of iron deficiency anemia is increased in the third trimester than the first and second trimester, the above mention fact was in agreement with NoronhaJA,BhaduriA.et,al 2010and Barrosa,Allards,KahanBc.et,al 201 Up to our knowledge there is no controversial idea regarding the above mention fact However this could be explain by the fact that the majority of women donot have adequate iron store to meets the dramatic increase in the requirement during the second till the third trimester (Let sky EA 1999 and Martin F 2009),also the most of iron transfer to fetus occurs during the third trimester (McDanagh M .et,al 2015), In fact the physiological drop in the hemoglobin in the second and the third trimester due to the higher increase in plasma volume (physiological hem dilution)is the most cause of(IDA)..(IdownOa.et,al 2005) In studying the influence of age in (IDA) this study showed the above 30 years old is mostly affected ,this findings further support the result of (Gomesda.et,al 2016),controversiallyBrunof, et.al ,2008 found that (IDA) more in female less than 20 years old .

Difference between this type of study and other types of studies is not surprising takinginto consideration the type of diet .medical care ,epidemiological factor ,and ethnic may contribute to the above reult.

Analyzing data of this study revealed significant difference in the prevalence of (IDA)in response to interpregnancy interval which is more in interval of 1-2 year than other groups ,this result is explain by the fact that iron stores of female are depleted during the course of pregnancy and lactation (William J.et,al 1995,Bruno F.et,al,2005 and OlusApi.et,al 2015).

Although there was no direct similar study to compare this study with others .This study provide evidence of iron deficiency anemia is more in female with less number of parity it's good to mention that disagreement with other authors that tested parity in various patient as example AnaGomes.et, al 2016, they found no correlation between parity and (IDA).sample size ,epidemiological factors and demographical factors may partly explain the controversial result .

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