ANAEMIA IN PREGNANCY

BARRY BENSTER
M.B., Ch.B., M.R.C.O.G.
Lecturer in Obstetrics and Gynaecology
Royal University of Malta

Anaemic women are a poor obstetric risk. They have an increased perinatal mortality and puerperal morbidity (Scott, 1961). Post partum haemorrhage is tolerated badly and if inadequately treated may result in maternal mortality or chronic ill health and reduced ability to cope with infant care and domestic responsibilities.

It is the purpose of this paper to assess the extent of the problem in Malta and to discuss some of the causes.

Materials and Methods

All patients attending the obstetric department at St. Luke's Hospital for the first time between January and July, 1968 are included. In addition patients were referred for the survey from government antenatal clinics.

Haemoglobin was estimated as cyanmethaemoglobin (Dacie and Lewis, 1963). Packed cell volume was measured using a Hawksley microhaematocrit centrifuge and reader. Statistical analyses were made according to Bailey (1959).

Results

The haemoglobin concentration was determined in 1010 patients; 403 of these had received some treatment before attending. This usually consisted of iron tablets for an average of 10 weeks. These treated patients are included, although shown separately in *Table 1* and *Figure 1*, as many of the published series record the haemoglobin levels at the first antenatal visit without selection. The inclusion of all patients here enables comparison to be made with the incidence in other centres.

The results show that 34 per cent of the untreated patients had a haemoglobin level less than 12 g. per 100 ml.

Before considering the effects of treatment it is necessary to assess other possible variables. *Tables 2-4* show the effect of age and parity on the haemoglobin concentration in the 607 untreated patients, and on the packed cell volume and mean corpuscular haemoglobin concentration in 459 of these.

Patients of parity 7+ had a significantly lower haemoglobin ($P < 0.001$) and a significantly lower packed cell volume

TABLE I

Percentages of untreated and treated Patients at different haemoglobin levels at first antenatal visit

(Number of patients in brackets)

Haemoglobin concentration (g. per 100 ml. blood)

	<9	9–9.9	10–10.9	11–11.9	12–12.9	13–13.9	14–14.9	15+	Total
Untreated	1.0 (6)	2.25 (14)	7.5 (45)	23.5 (143)	29.75 (180)	25.0 (152)	9.0 (54)	2.0 (13)	100 (607)
Treated	0.25 (1)	1.5 (6)	3.5 (14)	16.0 (65)	36.0 (145)	29.5 (119)	10.5 (42)	2.75 (11)	100 (403)
Total	0.7 (7)	2.0 (20)	5.8 (59)	20.6 (208)	32.2 (325)	26.8 (271)	9.5 (96)	2.4 (24)	100 (1010)

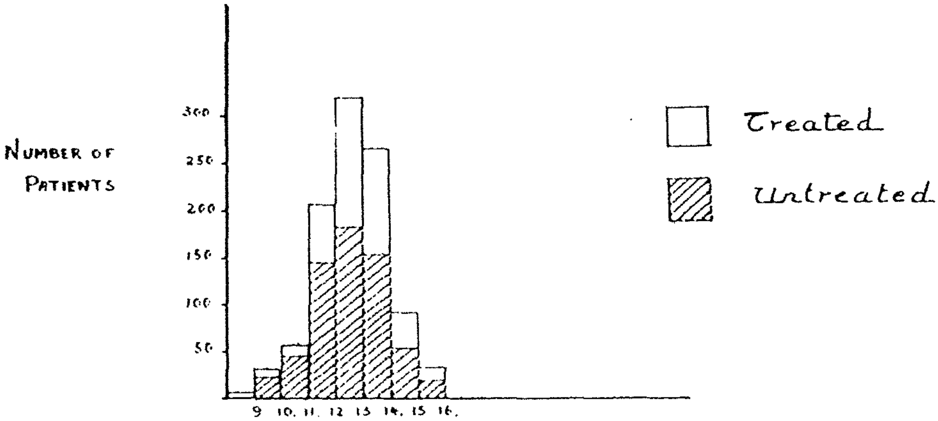

Fig. 1. Haemoglobin grams per 100 ml. Distribution of Haemoglobin Levels at First Antenatal visit

Fig. 1

(P < 0.01) than those of parity 0-6. This was not due to increasing age. The maximum haemoglobin concentration and packer cell volume occurred in the age group 25-29 and there was no appreciable decrease with increasing age.

The mean MCHC was very constant in the age and parity groups studied. The range was 31.7-32.0 per cent. The range of the haemoglobin levels was 11.8-12.7 g. per 100 ml. and packed cell volume 37.8-40.3 per cent.

The significant reduction in haemoglobin concentration and packed cell volume in the patients of para 7+ compared to para 0-6 could have been due to the grand multiparae attending later in pregnancy. This was not the case as may be seen from *Table 5.*

Discussion

Incidence

The incidence of anaemia in pregnancy in Malta is compared with surveys from other centres in *Table 6.* These figures allow only a very rough comparison which does not take into account age, parity, gestation or treatment. Several of the surveys were performed before the more accurate cyanmethaemoglobin method was introduced and in many the method used is not stated.

Iron requirements of pregnancy

The total permanent iron requirement of pregnancy varies from 474-1074 mg. (see *Table 7*).

There is some compensation from amenorrhoea amounting to about 120 mg. (Cheyne and Hytten, 1963). Elwood *et al.* (1968) collected menstrual blood and found that the mean iron content was 12.17 ± 1.67 mg. iron per period. If this figure is subtracted, then comparison with non-pregnant requirements can be made; but, as the iron loss of menstruation may be sufficient to cause anaemia, it is preferable to calculate the total iron requirement of pregnancy.

In addition to the permanent iron requirement it is necessary to consider the iron required for the normal increase in haemoglobin mass, which is 290-500 mg. (Hytten and Leitch, 1964; Rath *et al.*, 1950). This is a temporary demand as the iron is returned to the maternal stores after delivery. It has recently been reported that the iron stores of non-anaemic nulli-

TABLE 2
Effect of age and parity on haemoglobin concentration at first antenatal visit
Mean haemoglobin: g. per 100 ml. ± standard deviation
(Number of patients in brackets)

Age:	*15-19*	*20-24*	*25-29*	*30+*	*All ages*
Parity					
0	12.5 ± 0.9 (28)	12.5 ± 1.1 (104)	12.7 ± 1.3 (32)	12.2 ± 1.5 (19)	12.5 ± 1.1 (183)
1	12.35 ± 1.0 (4)	12.4 ± 1.6 (66)	13.0 ± 1.3 (42)	12.5 ± 1.5 (28)	12.6 ± 1.5 (140)
2-3	—	12.2 ± 1.4 (27)	12.5 ± 1.4 (41)	12.5 ± 1.4 (65)	12.5 ± 1.4 (133)
4-6	—	12.5 ± 0.9 (5)	12.5 ± 1.1 (21)	12.5 ± 1.3 (74)	12.5 ± 1.3 (100)
7+	—	—	12.2 ± 0.9 (5)	11.8 ± 1.4 (46)	11.8 ± 1.4 (51)
Group mean	12.5 ± 0.9 (32)	12.4 ± 1.3 (202)	12.7 ± 1.0 (141)	12.3 ± 1.4 (232)	12.5 ± 1.3 (607)

TABLE 3
Effect of age and parity on packed cell volume at first antenatal visit
Mean packed cell volume, per cent ± standard deviation
(Number of patients in brackets)

Age	*15-19*	*20-24*	*25-29*	*30+*	*All ages*
Parity					
0	39.7 ± 2.6 (15)	39.1 ± 3.2 (90)	40.3 ± 3.0 (22)	38.9 ± 3.2 (14)	39.3 ± 3.0 (141)
1	37.5 ± 2.7 (4)	38.8 ± 4.3 (50)	41.5 ± 2.8 (33)	40.1 ± 4.5 (20)	39.8 ± 4.0 (107)
2-3	—	38.1 ± 3.4 (15)	40.1 ± 4.2 (29)	38.6 ± 4.2 (49)	39.0 ± 4.1 (93)
4-6	—	39.0 ± 4.4 (5)	38.9 ± 2.9 (15)	39.9 ± 3.6 (54)	39.6 ± 3.5 (74)
7+	—	—	37.5 ± 2.9 (4)	37.8 ± 3.7 (40)	37.8 ± 3.6 (44)
Group mean	39.2 ± 2.7 (19)	38.9 ± 3.5 (160)	40.3 ± 3.4 (103)	39.0 ± 3.9 (177)	39.3 ± 3.7 (459)

TABLE 4
Effect of age and parity
on Mean corpuscular haemoglobin concentration (M.C.H.C.)
at first antenatal visit
M.C.H.C. per cent ± standard deviation
(Number of patients in brackets)

Age / *Parity*	*15-19*	*20-24*	*25-29*	*30+*	*All ages*
0	31.8 ± 2.0 (15)	31.8 ± 1.4 (90)	31.75± 2.0 (22)	31.4 ± 2.2 (14)	31.8 ± 1.6 (141)
1	32.9 ± 1.0 (4)	31.9 ± 2.0 (50)	31.9 ± 1.6 (33)	31.7 ± 1.9 (20)	31.9 ± 1.8 (107)
2-3	—	31.7 ± 1.5 (15)	31.6 ± 1.7 (29)	32.3 ± 2.1 (49)	32.0 ± 1.9 (93)
4-6	—	32.2 ± 1.7 (5)	32.3 ± 2.1 (15)	31.7 ± 2.0 (54)	31.9 ± 2.0 (74)
7+	—	—	33.8 ± 1.4 (4)	31.1 ± 1.7 (40)	31.7 ± 2.1 (44)
Group mean	32.0 ± 1.9 (19)	31.9 ± 1.6 (160)	31.9 ± 1.8 (103)	31.7 ± 2.0 (177)	31.8 ± 1.9 (459)

parous women are as low as 254 mg. (range 59-502 mg.) (Pritchard and Mason, 1964). If this is correct, then it is not surprising that these stores are frequently insufficient to meet even the temporary demand for iron to increase the maternal haemoglobin mass.

The iron requirement for lactation is not considered in *Table* 7. Scott (1962) states that an extra 180 mg. of iron is required. Estimates for human milk have varied from 0.25 mg. per day (Macy and Kelly, 1961) to 3.1 mg. per day (Reis and Chakmakijian, 1932). The duration of lactation is very variable. Of 100 consecutive patients who attended the clinic for postnatal haemoglobin investigation only 28 per cent were still breast feeding after six weeks.

TABLE 5
Duration of pregnancy
at first attendance according to parity

Parity / *Gestation*	*0-6*	*7+*	*Total*
0-20	200	17	217
21-30	134	15	149
31-42	222	19	241
Total	556	51	607

Iron absorption

It has been estimated that between 5 and 10 per cent, or 0.6-1.5 mg., of the iron is absorbed from a daily intake of 12-15 mg. (Moore, 1964).

There is some evidence that in pregnancy iron absorption is increased, and possibly trebled during the third trimester (Hahn, 1951). If the iron required for pregnancy, i.e. 474-1074 mg., is absorbed evenly throughout, it will amount to about 1.7-4 mg. per day, and even if iron absorption is trebled in the third trimester then the 1.8-4.5 mg. that may be absorbed is barely sufficient to meet these requirements.

Blood volume changes

Anaemia is usually defined as a reduction in the haemoglobin concentration in

TABLE 6

Incidence of anaemia in pregnancy
Haemoglobin level below 10 g.

Centre	*Authors*	*Method*	*No. of Patients*	*Percentage Incidence*
Vellore, India	Baker (1966)	—	200	40
Trinidad	Chopra *et al.* (1967)	cyanmethaemo-globin	555	34
Dublin	Doyle & McGrath (1954)	—	1000	31.4
Louisiana, U.S.A. *	Lund (1951)	oxyhaemoglobin	4015	20
Hong Kong	Todd & Kan (1965)	oxyhaemoglobin	1915	14.5
London, East End	Steingold (1966)	—	—	9.0 (< 10.2)
Jerusalem	Strauss *et. al.* (1961)	—	2498	6.9
Australia	Walsh (1953)	—	—	3.0
Malta	Present Series	cyanmethaemo-globin	1010	2.7
Aberdeen	Turnbull (1956)	—	—	2.4 (< 10.4)
Pretoria, S. Africa **	Theron *et al.* (1961)	—	194	2.0
		Haemoglobin level below 12 g.		
Jamaica	Pathak *et al.* (1967)	—	1000	55
Malta	Present Series	—	1010	29
Newcastle, England	Thompson (1965)	—	1000	17.4

* Low income group.
** Bantu.

the blood. In pregnancy the diagnosis is complicated by the changes that occur in plasma and red cell volume. Paintin, Thompson and Hytten (1966) consider that a decrease in haemoglobin concentration is inevitable as the plasma volume always increases more than the red cell volume.

Low, Johnson and McBride (1965) reviewed the studies of plasma and red cell volume changes in pregnancy reported by Thomson *et al.* (1938), Roscoe and Donaldson (1946), Caton *et al.* (1949, and 1951), McLennan and Thouin (1950), Tysoe and Lowenstein (1950), Adams (1954), and Pritchard (1960).

The results with number of patients in brackets were as follows:

	Plasma Volume	*Red Cell Volume*
Mean level for non-pregnant patient	2572 (80)	1941 (97)
Mean level in third trimester	3628 (134)	1767 (159)
Increase in pregnancy	1056 41%	276 18.5%

These pooled results show that there is a greater increase in mean plasma volume than red cell volume in pregnancy, but assessment of mean levels fails to indicate the proportion of patients whose plasma volume increase exceeds the red cell volume increase.

Recent studies have indicated that

red cell volume increase in pregnancy is largely dependent on the adequate provision of iron. Plasma volume increase is very variable and unpredictable though it does not seem to be dependent on the supply of iron (de Leeuw *et al.*, 1966). In a study of 100 pregnant women with a haemoglobin level less than 4 g. per 100 ml. it was found that the plasma volume was similar to that in pregnant non-anaemic controls, though the red cell mass was considerably reduced (Vyas *et al.*, 1968).

It is not possible to determine the extent to which iron deficiency contributed to the failure of red cell volume increase in the above pooled results.

In view of the controversy as to the extent to which hypervolaemia influences the haemoglobin level in pregnancy in the absence of iron deficiency, the findings of Whiteside (1960) are of particular interest.

He investigated 23 pregnant women. All were treated with iron. Twelve maintained a constant haemoglobin and had a proportionate increase in red cell and plasma volume. In the remaining 11 patients a significant fall in haemoglobin level occurred and this was associated with an excessive rise in plasma volume and a normal rise in red cell volume. All patients had normal serum iron levels.

This is a small series and it indicates that hypervolaemia may occur in the absence of iron deficiency, though probably in less than 50 per cent of patients.

The position is by no means clear and further work is required to assess the importance of hypervolaemia in pregnancy. There are several problems specifically related to pregnancy that have to be overcome if a successful study is to be achieved: lean body mass which correlates best with blood volume is not easily measured in pregnancy, repeat estimations with isotope techniques are not justified in view of the radiation hazard to the foetus, and water retention and oedema may complicate the result (Duhring, 1964).

It is of interest that in the present series the mean corpuscular haemoglobin concentration remained very constant compared with the haemoglobin and packed cell volume. This suggests that a relatively greater increase in plasma to red cell volume has played some part in lowering the haemoglobin concentration and packed cell volume equally.

In view of the unpredictable variation in plasma volume and the high incidence

TABLE 7

Iron required for pregnancy

	Iron (mg.)	*Author*
Placenta and cord *	34.5 — 170	McCoy *et al.* (1961)
Foetus **	200 — 374	Widdowson *et. al.* (1951)
Blood loss at delivery	100 — 250	Moore (1964)
Iron loss in urine, faeces and sweat	140 — 280 (0.5 — 1.0 mg. per day)	Moore (1964)
Total permanent iron requirement	474.5 — 1074	
Temporary iron requirement for increase in haemoglobin mass	290 — 500	Hytten & Leitch (1964) Rath *et al.* (1950)
TOTAL iron requirement	764.5 — 1574	

* 46 placentae and cords.
** 6 stillbirths or neonatal deaths. Weight more than 3000 g. (possibly not representative of the normal foetus).

of iron deficiency in pregnancy it is safer to consider that any significant reduction of haemoglobin concentration in pregnancy is probably abnormal. When hypervolaemia is suspected in view of the poor response to therapy then the estimation of packed cell volume and mean corpuscular haemoglobin concentration is of value.

Summary

A survey of anaemia in pregnancy in Malta revealed that 33 per cent of untreated patients first attending the antenatal clinic had a haemoglobin concentration of less than 12 g. per 100 ml.

Patients of very high parity had a significantly lower haemoglobin and packed cell volume.

Mean corpuscular haemoglobin concentration remained very constant in the age and parity groups studied.

A review of iron balance and blood volume studies in pregnancy suggests that iron deficiency is likely to be an important cause of the high incidence of anaemia.

Packed cell volume and mean corpuscular haemoglobin concentration are of value in assessing the extent of hypervolaemia in pregnancy.

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