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Research Paper

Anaemia Among Gynaecological In-Patients In A Tertiary Health Centre In Southern Nigeria

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Abstract
Objective: *To study the incidence, pattern and treatment of anaemia amongst gynaecological in-patients at the University of Benin Teaching Hospital.*
Methods: *The data of all patients admitted into the gynaecology ward from 1st January to 31st December 2019 were prospectively obtained, employing a self-designed study proforma. The haemoglobin levels of all patients were estimated at admission and discharge and their treatment followed up to their discharge. Data obtained was analyzed using SPSS 21.* ***Results:*** *The incidence of anaemia during the study period was 71.5%. Gestational trophoblastic disease had the least haemoglobin level at admission. Anaemia was commoner in premenopausal women at presentation compared to postmenopausal women (84.2% versus 15.8% p = 0.07) but there was a statistically significant difference in anaemia between premenopausal women and postmenopausal women at discharge (84.1 versus 15.9, p < 0.001). There was also significant difference in the transfusion trigger at haemoglobin level ≤6.0g/dl for premenopausal compared to postmenopausal (92 versus 8% p = 0.002) and those who had infection as co-morbidity (p = 0.02) and also those who had chemotherapy as treatment modality (p = 0.04). There was no difference between the two strata of women regarding transfusion as a mode of management of anaemia.* ***Conclusion:*** *Anaemia is common among gynaecology in-patients due to factors consequent on the etiopathogenesis of the disease and sometimes the treatment of the disease itself. All patients admitted as anaemic were discharged the same due to the restrictive transfusion strategy employed and the haemoglobin level benchmark of 12g/dl set by the World Health Organization.*
Keywords: *Anaemia, haemoglobin, gynaecological inpatients, transfusion trigger.*

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I. INTRODUCTION

Anaemia has endured as a major public health concern worldwide, commonly among females of reproductive age and beyond and this is more so in resource-limited countries. Anaemia is a condition in which the number of red blood cells (and consequently their oxygen-carrying capacity) is insufficient to meet the body's physiologic needs [1]. The Specific physiologic needs vary with a person's age, gender, residential elevation above sea level (altitude), smoking behaviour, and different stages of pregnancy [1].

According to the World Health Organization (WHO), anaemia is considered to exist at haemoglobin levels lower than 12g/dl in women [1]. However, there is significant variation in the distribution of normal haemoglobin and this depends on the environment, sex, race, culture and physiological status [2]. New lower limits of normal haemoglobin values have been suggested, according to ethnicity, gender, and age [2] and [3]. Anaemia is often multifactorial and is not an independent phenomenon [3].

Recent studies have called into question this definition by WHO, which nevertheless remains the gold standard for epidemiologic and clinical studies, as well as for objective clinical practice [3] and [4]. A critical issue concerns whether to use different normal values for postmenopausal and elderly women. Baducci et al [4] noted that "ageing is associated with a progressive reduction in hemopoietic reserve due to exhaustion of pluripotent stem cells, increased circulation of catabolic cytokines, and possible alterations in the microenvironment and the production of hemopoietic growth factors. In many respects, hemopoiesis may reflect general age-related changes" [4].

The global estimate of anaemia prevalence averaged 56% with a range of 35-75% depending on geographic locations [2]. Prevalence of anaemia in Sub-Saharan Africa is among the highest in the world, mirroring overall; high rates of poverty and malnutrition [5]. In Nigeria, the prevalence rate was 62% [6]. The incidence and prevalence of anaemia increase with age and are highest in institutionalized populations [7] and [8]. For social, racial and economic reasons, nutritional anaemia is more prevalent in 3rd world countries [1]. Similarly, anaemia of chronic disorders is prevalent in the population with a high incidence of chronic infestations (helminthiasis) and diseases such as malaria, tuberculosis and acquired immune deficiency syndrome [9].

While anaemia consequent on acute or chronic blood loss is established, anaemia related to "the progress of cancer results from the cumulative effects of inflammation and the immune system. The results of which lead to impaired utilization of iron, suppression of erythroid progenitor cell differentiation, and inadequate erythropoietin production" [10]. Cancer-related anaemia is a sign that may complement the progression of cancer itself and is frequently diagnosed in patients at advanced stages. It can ensue independently after administration of antineoplastic drugs. Patients with cancer have been shown to have inappropriately low levels of circulating erythropoietin for their degrees of anaemia [11]. Furthermore, the lifespan of red blood cells is also shortened in cancer-related anaemia and the production of new cells cannot compensate for the shortened survival time [11] and [12]. Some cancers are associated with revealed or concealed bleeding or both.

Factors likely to increase the risk of anaemia in cancer patients include the type, shape, duration of the disease, treatment regimen and intensity, presence of infection and the need for surgical intervention [11]. The prevalence of anaemia appears to be especially high in patients with uterine–cervical cancers and those suffering from cancer-related renal impairment [10]. "Almost all patients with cancer develop mild anaemia after chemotherapy and about 80% experience more serious anaemia" [13] and [14].

The ability of a patient to tolerate anaemia depends on her clinical condition and the presence of any significant co-morbidity. Anaemia initiates reduced quality of life as it causes palor, fatigue, dizziness, tachycardia, impaired renal function, heart failure, functional and cognitive decline, especially in older patients [8] and [12]. In cancer patients, anaemia enhances the risk of chemotherapy-induced toxicity and reduced response to treatment [15]. The response of cervical cancer to radiation therapy was reduced in patients with anaemia [16].

Transfusion of red blood cells is a swift and dependable method of managing anaemia, especially in emergent and life-threatening circumstances. However, significant variations subsist in red blood cell transfusion carried out in routine and emergent care [17]. While there is no universal transfusion trigger, "current guidelines for critically ill and pre-operative patients advised that, at haemoglobin values of 7g/dl, red blood cell transfusion is strongly indicated whereas, at values greater than 10g/dl, blood transfusion is unjustified. For patients with haemoglobin values in the range of 7-10g/dl, the transfusion trigger should be based on clinical indicators and physician consideration" [17] and [18]. However, uncertainties still exist concerning the most appropriate haemoglobin concentration for patients with significant cardiorespiratory disease [19].

The other issue in red blood cell transfusion in critically ill patients is the use of restrictive versus liberal red blood cell transfusion. Herbert et al [20] and [21] and Vincent et al [11] working independently reported: "that neither mortality nor development of organ dysfunction was affected by the transfusion strategy but using restrictive strategy was at least as effective as and superior to a liberal transfusion strategy with the possible exception of patients with acute myocardial infarction and unstable angina". Transfusion of blood is associated with infections, transfusion reactions and worsened cancer outcome [11].

Where anaemia is not life-threatening it is advocated, that it should be managed with hematinics and erythropoietin [15]. Erythropoietin and erythropoietin stimulators; epoetin alpha and beta, and darbepoetin reverse anaemia due to relative erythropoietin insufficiency especially in cancer patients [15] and [16]. Seidefeld et al [22] reported that epoetin therapy reduced the percentage of patients transfused by 7−47% while Dunphy et al [23] found a 50% reduced need for transfusion. Littlewood and colleagues noted a significant decrease in transfusion requirement in patients receiving non-platinum chemotherapy and epoetin compared to those receiving only chemotherapy [24].

The essential nature of anaemia in medical practice and the dearth of study among gynaecological patients in our environment prompted the interest to (i) examine anaemia between the different gynaecological diseases, (ii) examine the impact of the treatment modalities on anaemia in gynaecological patients and (iii) investigate the pattern of anaemia between women in the reproductive age and postmenopausal women.

II. MATERIALS AND METHODS

This was a prospective cross-sectional study involving women admitted into the gynaecology ward of the University of Benin Teaching Hospital, Benin City between January 1st and December 31st, 2019.

All gynaecological patients admitted into the ward in the period under review were enrolled into the study at admission and followed up until they were discharged. The haemoglobin levels at admission and discharge, the treatment modalities including antineoplastic drugs and the units of blood transfused for each patient were collected and entered into a self-designed study proforma. The haemoglobin levels were determined using the HemoCue Hb 801 haemoglobin photometer method. The middle or the ring fingers were used after they have been cleaned with methylated spirit and then wiped dry. A puncture at the tip of the finger was made with a lancet and the first 2 to 3 drops of blood were wiped away and the finger was gently squeezed until there were drops of blood enough to fill the microcuvette. The microcuvette was used to collect the blood ensuring that it is properly filled and there were no bubbles. It is then placed in the Hemocue machine and the result recorded. All co-morbidities were duly investigated and appropriate treatment modalities were instituted.

Excluded from the study were; (1) patients with ovarian hyperstimulation syndrome due to the frequent variability of their haemoglobin levels with haemoconcentration. (2) Patient with a known medical history of bleeding disorder and (3) patient with haemoglobinopathies.

Anaemia was defined using the WHO value of lower than 12g/dl. Statistical analysis was performed with the SPSS software (statistical package for social sciences, SPSS v 19.0, Chicago, IL). Statistical significance was ascertained using the chi-square test, *p*-value at 0.05 was considered significant.

III. RESULTS

Table 1: Sociodemographic characteristics of the patients

Characteristics	Number	Percentage
Age (years)		
15 – 19	16	3.9
20 – 29	142	34.2
30 – 39	131	31.6
40 – 49	52	12.5
50 – 59	34	8.2
60 – 69	20	4.8
70 – 79	18	4.3
80 – 89	2	0.5
Educational Status		
No formal education	37	8.921.7
Primary	90	34.5
Secondary	143	34.9
Tertiary	145	
Reproductive Age		
Premenopausal	349	84.1
Postmenopausal	66	15.9

A total of 415 patients were analyzed. Single, married and widow patients were 117, 264 and 34 with corresponding percentages of 28.2, 63.6 and 8.2 respectively.

Christians accounted for 98.1%, Moslem 0.5% and Jehovah's Witness 1.4% of the total patients analyzed.

Table 2: Haemoglobin level and its distribution among disease conditions, duration of hospital stay and blood transfusion

characteristics	number	% of total	Mean admitting Hb level	Mean Hb level at discharge	Mean units transfused	Duration of hospital stay (days)
Abortions	52	12.5	9.8 ± 2.3	10.1 ± 1.5	1.7 ± 2.2	6.7 ± 8.1
Ectopic pregnancy	82	19.8	8.5 ± 2.2	9.6 ± 0.2	2.0 ± 1.6	5.6 ± 0.8
Ovarian cyst	38	9.2	11.2 ± 1.5	10.1 ± 1.5	0.4 ± 0.9	7.8 ± 6.8
Uterine fibroids	82	19.8	11.3 ± 2.0	10.1 ± 1.0	0.9 ± 1.6	6.4 ± 1.2
Endometrial Polyps	7	1.7	11.0 ± 0.6	10.1 ± 0.8	1.7 ± 2.5	3.2 ± 0.8
*GTD	26	6.3	7.9 ± 1.5	9.8 ± 0.6	4.7 ± 2.6	20.5 ± 15.4
Endometriosis	2	0.5	10.0 ± 2.4	10.1 ±1.1	1.7 ± 2.5	5.6 ± 1.4
Endometrial CA	4	1.0	10.8 ± 1.7	10.7 ± 0.4	1.0 ± 1.2	8.0 ± 1.6
Cervical CA	57	13.7	9.6 ± 2.5	10.2 ± 0.9	2.1 ± 2.8	6.0 ± 3.4
Ovarian CA	31	7.5	10.0 ± 2.4	10.1 ± 0.5	3.5 ± 3.2	22.7 ± 12.6
Vulva CA	2	0.5	9.6 ± 2.5	10.2 ± 0.9	2.1 ± 1.6	6.1 ± 3.4
VVF	26	6.3	11.6 ± 0.7	11.1 ± 1.0	1.8 ± 0.5	14.0± 4.8
All Cases	415	100	10.0 ± 2.3	10.1 ± 1.1	1.7 ± 2.4	9.1 ± 9.6

** GTD = Gestational trophoblastic disease ⁺VVF = Vesico-vaginal Fistula. CA = Carcinoma*

The above table shows that patients with gestational trophoblastic disease (GTD) as well as those with ectopic pregnancy had the lowest haemoglobin levels on admission (7.9 ± 2.3 vs 8.5 ± 2.2) and received the highest units of blood transfusion (4.7 ± 2.6 vs 2.0 ± 1.6). Ectopic pregnancy and gestational trophoblastic disease had the lowest haemoglobin level at discharge (9.6 ± 0.2 and 9.8 ± 0.6 respectively). Ovarian carcinoma and gestational trophoblastic disease had the longest hospital stay.

Table 3: Haemoglobin level and transfusion trigger in reproductive age compared with postmenopausal women.

Characteristics	Number	% of total	Women of reproductive age (%)	Postmenopausal women (%)	*P*-value	Chi-square
Hb Level at admission						
≥12.0g/dl	92	28.5	77(83.7)	15(16.3)	0.008	27.01
≤11.9g/dl	323	71.5	272(84.2)	51 (15.8)	0.07	40.00
Hb Level at discharge						
≥12.0g/dl	24	5.8	20 (83.7)	4(16.3)	0.46	6.72
≤11.9g/dl	391	94.2	329(84.1)	62(15.9)	<0.001	49.02
Transfusion Trigger						
≥6.0g/dl	50	26.3	46(92.0)	4(8.0)	0.002	26.22
6.1 – 9.0g/dl	140	73.7	106(75.7)	34 (24.3)	0.20	14.68
No of units transfused						
1 – 2	65	34.2	53(81.5)	12(18.5)	0.67	0.19
3 – 4	79	41.6	64 (81.0)	15 (19.0)	1.00	0.006
>5	46	24.2	34 (73.9)	12(26.1)	0.48	0.50

The prevalence of anaemia using the WHO criteria of 12.0g/dl was 71.5%. Premenopausal women were more likely to be admitted with normal haemoglobin levels (≥12.0g/dl) compared to postmenopausal women (*p-value* = .008) and they are also more likely to be discharged as anaemic (Hb ≤11.9g/dl) *p-value*= <.001.Premenopausal patients were more likely to be admitted with severe anaemia (Hb ≤ 6.0g/dl) compared with postmenopausal patients (90 versus 10% *p-value* = 0.002). No statistical difference between the number of units of blood transfused between both groups when 1 to 2 and >5 units of blood is transfused.

Table 4: Comorbidities/treatment modality complicating anaemia among the patients

Characteristics	Yes (%)	No (%)	*P*-value
Malaria	30(9.3)	292 (90.7)	0.53
Infection	35(10.8)	288(89.2)	0.02
HIV	19(5.9)	304(94.1)	0.76
Gastrointestinal loss	1(0.4)	322(99.6)	1.00
Chemotherapy	42(13.0)	281(87.0)	0.04
Haemoglobinopathy	2(0.6)	321(99.4)	1.00

There was a statistically significant difference in infection as a co-morbidity (P=0.02) and chemotherapy as a treatment modality (P=0.04) in complicating anaemia.

Table 5: Mode of treatment of anaemia in reproductive age compared with postmenopausal patients

Characteristics	Number	% of total	Women of reproductive age (%)	Postmenopausal women (%)	P-value	Chi-square
Bl. transfusion	190	45.8	152 (80.6)	38 (19.4)	0.04	4.40
Haematinics alone	217	52.3	187 (86.6)	29 (13.4)	0.10	2.22
Haematinics + bl.Tx*	190	45.8	152 (80.6)	38 (19.4)	0.0	2.22
Parenteral iron	0	0	0 (0)	0 (0)	—	—
Erythropoietin	0	0	0 (0)	0 (0)	—	—
Observation	8	1.9	8 (100)	0 (0)	0.004	8.08

**Tx = Transfusion*

There was a statistically significant difference in terms of blood transfusion between women of reproductive age and postmenopausal women (80 versus 20% $p = 0.04$). There was no statistically significant difference between premenopausal and postmenopausal women in terms of mode of treatment using hematinics alone (86.6 versus 13.4%, $p = 0.104$) and hematinics with blood transfusion (80.6 versus 19.4%, $p = 0.107$). No patient was managed with erythropoietin or parenteral iron.

There was also a statistically significant difference between women of reproductive age and postmenopausal women when no treatment (observation) was instituted in the management of anaemia (100% vs.0% *p*-value = 0.004). No patient had erythropoietin/its derivatives or parenteral iron.

IV. DISCUSSION

Employing the benchmark of 12.0g/dl prescribed by the World Health Organization, the incidence of anaemia in this study is 71.5% and this is consistent with the reports by other authors [2], [9] and [20] but was higher than the reports by other researchers [6] and [22]. The high incidence recorded can be attributed majorly to two factors: (i) the cases of active bleeding per vaginam at presentation, in this scenario a large number of the cases may already be anaemic at presentation due to haemorrhage and (ii) due to the hyperendemicity of malaria in our environment such that some patients that were bleeding were already anaemic [25].

All the patients admitted as anaemic were all discharged anaemic despite treatment and or transfusion. The combination of no transfusion undertaken at haemoglobin level 10–12g/dl and the maximum transfusion trigger set at haemoglobin level 6.1–9g/dl implies that the restrictive transfusion strategy was practiced. This is consistent with the reports of other authors [6], [11], [16] and [17]. The practice of the restrictive transfusion strategy is the reason, all the patients were discharged anaemic. Best practice dictates that "the decision to embark on blood transfusion is a composite one which involves cognizance of the haemoglobin level, overall clinical context, prevention of blood-borne infections, patient consent and preferences and consideration of alternative therapies"[18] and[17]. When transfusion is to be undertaken the restrictive red blood cell transfusion approach is recommended as was seen in the study [22]. All patients that were transfused had hematinics to enable the body to build and correct the residual anaemia.

This study demonstrated that gestational trophoblastic disease followed by ectopic pregnancy are the gynaecological disease conditions that are most likely to present with the most severe forms of anaemia. This is so because these conditions are associated with rapid haemorrhage, while gestational trophoblastic disease and ovarian carcinoma are the more likely diseases to require transfusion with higher units of blood. This may be so partly because our hospital is a referral one and partly because erythropoietin was not used in the management of patients with cancer. The latter two disease conditions are also associated with chronic anaemia and a longer period of hospital stay.

The study also revealed no increased risk of anaemia in postmenopausal women compared to women of the reproductive age group. This substantiates the report by Inelmen *et al* [25]. Premenopausal women are more likely to be discharged anaemic compared to postmenopausal women. This was largely due to gestational trophoblastic disease and ectopic pregnancy which causes the highest severity of anaemia occurring exclusively in this group. However, with the advent of *in vitro* fertilization, these diseases will certainly occur in postmenopausal women.

Despite the proven benefits of erythropoietin in the management of anaemia in cancer patients [22] and [23] none was used, due partly to dearth, cost and sustainability. Certainly, combining it with chemotherapy will increase the cost of treatment and this will poise the challenge of sustainability. Parenteral iron was also not used as a modality of treating anaemia because it has no superior therapeutic effect over oral iron in terms of raising the haemoglobin level and is associated with anaphylactic reactions, infusion site reactions, such as pain, extravasation and injection site staining, injection abscess and necrosis [26].

Infections and chemotherapy were the only significant contributors to anaemia in this study. Similar findings have been reported by other authors [26] and [27]. Despite the endemicity of malaria in our environment, it was not a significant co-morbidity causing anemia in this study because it was promptly screened for in patients with fever and appropriate treatment was instituted.

V. CONCLUSION

Anaemia among gynaecological patients was high and this is as a result of environmental factors and factors inherent in the etio-pathogenesis of the diseases. For the considered disease/conditions, premenopausal women are more likely to be admitted and discharge with anaemia compared to postmenopausal women. The use of the restrictive transfusion strategy invariably portends that all gynaecological patients requiring transfusions to correct anaemia will be discharged as anaemic.

LIMITATIONS

The findings of the study are hospital-based and as such cannot be extrapolated to the general population even though the hospital serves as a referral to other peripheral hospitals. The proportion of nutritional anaemia contributing to the overall picture of anaemia cannot be overlooked more so when the poverty level in our locality and Nigeria is considered. The non-usage of erythropoietin and erythropoietin stimulators may have impacted the results. Its use may have reduced the risk of blood transfusion.

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