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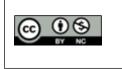
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MATERNAL AND PERINATAL MORBIDITY AND MORTALITY IN ANAEMIA DURING PREGNANCY

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Abstract

Background: Anaemia is defined by World Health Organization as haemoglobin concentration < 11gm/dl and haematocrit less than 33%. World Health Organization has estimated that prevalence of anaemia in pregnant women is 65-75% in India. Identification of reversible factors such as anaemia which is a treatable condition will be of great help for prioritization of interventions so that risk management strategies can be done. Materials and Methods: The patients included in the study were antenatal anaemic patients 28 weeks onwards in labour. Baseline investigations were carried out in all patients. Maternal and perinatal outcome was noted at the time of delivery and assessed as antenatal infections, postnatal infections, Post-Partum Hemorrhage, Pregnancy-induced hypertension, subinvolution of uterus, failure of lactation, preterm, Low Birth Weight, Apgar score, requirement for Neonatal intensive care unit, Intrauterine Death and maternal mortality. Result: In our study, out of 103 patients, majority of the study population had moderate anaemia 54.4%. The mean haemoglobin level was 7.15 gm/dl. Majority of patients were 3rd gravida 33.00%. 16.5% patients had antenatal infections. 34.95% patients had postnatal infections. Significant association was seen between anaemia and infections. 24.3% patients had Post-Partum Hemorrhage, which was significant. 30.09% patients had PREGNANCY-Induced Hypertension. 8.8% patients had subinvolution of uterus and 6.8% patients had failure of lactation, both highly significant. 38.83% babies were preterm. 67.96% babies were LOW BIRTH WEIGHT. 21.35% babies had Apgar score < 7 and had requirement for NEONATAL INTENSIVE CARE UNIT which was significant. 16.5% babies were INTRAUTERINE DEATH and Out of 103 patients, maternal mortality was 7.8%, and both significantly associated with maternal anaemia. Conclusion: Maternal anaemia is an increasing cause of INTRAUTERINE DEATH, LOW BIRTH WEIGHT, Preterm delivery and NEONATAL INTENSIVE CARE UNIT admissions. Timely identification of women with maternal anaemia and associated maternal and fetal complications like antenatal infections, postnatal infections, POST PARTUM HEMORRHAGE, PREGNANCY-INDUCED HYPERTENSION, subinvolution of uterus, failure of lactation, preterm, LOW BIRTH WEIGHT, requirement for NEONATAL INTENSIVE CARE UNIT, INTRAUTERINE DEATH and maternal mortality can help in reducing maternal morbidity and mortality.

INTRODUCTION

Anaemia is defined by the World Health Organization as hemoglobin concentration of $< 11 \text{gm/ dl},^{[1,2]}$ and a hematocrit of less than 33%. The prevalence of anemia in India varies from 55% to 75%,^[3] World Health Organization has estimated that prevalence of anaemia in pregnant women is 14% in developed and 51% in the developing countries and 65 – 75% in India. In India, the prevalence of anaemia is high because of fewer intake of iron, folic acid and food sources that prevent iron absorption, coupled with poor bioavailability of iron is the major factor responsible for prevalence of anemia.^[4-15] Maternal risks in anaemia increase prior to the fetal risks. Anaemia is responsible for 40% of maternal mortality directly or indirectly.^[4,6] There is 8 to10 fold increase in maternal mortality rate (MMR) when hemoglobin falls below 5g/dl.

Grading of anaemia in pregnancy [World Health Organization] –^[7]

- Mild anaemia: Hemoglobin 9-10.9 gm/dl
- Moderate anaemia: Hemoglobin 7-8.9 gm/dl
- Severe anaemia: Hemoglobin <7 gm/dl
- Very severe: Hemoglobin <4 gm/dl

Mild and moderate anemia leads to weakness, lack of energy, fatigue, poor work performance. Severely anaemic patients are more susceptible to infections, hemorrhage [Post-Partum Hemorrhage] causing cardiac failure and subsequently leading to maternal death.^[8]

Available data from India indicate that maternal morbidity rates are higher in women with Hemoglobin below 8.0 g/dl. Maternal mortality rates show a steep increase when maternal Hemoglobin levels fall below 5.0 g/dl.^[9] Anaemia directly causes 20 percent of maternal deaths in India and indirectly accounts for another 20 percent of maternal deaths.^[10,11] A study by the World Health Organization (WHO) documented that severe antenatal or postnatal maternal anemia (of any type) was associated with an increased risk of maternal and fetal complications. Thus identification of reversible factors such as anemia in pregnancy which is a treatable condition will be of great help for policy making and clinical purpose such as prioritization of interventions so that more intensive observation and improvement of risk management strategies can be done.^[12]

MATERIALS AND METHODS

This was a hospital based cross sectional study to observe the effects of maternal and perinatal morbidity and mortality in anaemia during pregnancy. In this study the antenatal anaemic patients of gestational age 28 weeks onwards in labour visiting Obstetrics and Gynaecology department for a period of 18 months were included, which was 103 in number. An informed and written consent was obtained before including them in the study. Baseline investigations were carried out in all patients. Detailed history, presenting complaints, general, systemic and obstetrical examination findings were recorded. Special emphasis was given to ascertain the cause of anaemia. Period of gestation at the time of delivery, any indication for induction or augmentation of labor, mode of delivery was recorded.

Patients with chronic medical illness like (Patients with active tuberculosis, diabetes mellitus, pregnancy induced hypertension, pre-eclampsia toxemia, chronic obstructive pulmonary disease), Patients with history of repeated blood transfusion, Known patients of thalassemia, malignancy, Patients not willing to be part of study were excluded from study.

Maternal and perinatal outcome was noted at the time of delivery and outcomes were assessed as antenatal infections, postnatal infections, postpartum haemorrhage, Pregnancy-Induced Hypertension, subinvolution of uterus, failure of lactation, preterm, low birth weight, Apgar score, requirement for neonatal intensive care, intrauterine death (IUD) and maternal mortality.

RESULTS

In our study, out of 103 patients, majority of the study population had moderate anaemia 54.4% followed by 35% had Severe Anaemia, 6.8% had Very Severe Anaemia and 3.9% had Mild Anaemia [Table 1]. The mean haemoglobin level in present study is 7.15 gm/dl. The mean age group in present study is 27 years. Majority of anaemic patients were 3rd gravida 33.00% followed by 4th Gravida (30.09%), 2nd Gravida (19.41%), 1st Gravida (10.67%), 5th Gravida (3.9%), 6th Gravida (2.9%). 54.4% patients did not take any Haematinics (Iron, Folic Acid, Vitamin B12 Supplements) during pregnancy, 47% patients had taken Haematinics during pregnancy. 16.5% patients had antenatal infections. 34.95% patients had postnatal infections [Table 4,5]. Significant association was seen between anaemia and infections. (p value <0.001, chi square 33.80).

24.3% patients had postpartum haemorrhage [Table 3], Association of anaemia with postpartum haemorrhage was significant (p value 0.027, chi square value 9.20). In Our Study Pregnancy-induced hypertension was present among 31/103 (30.09%) of mothers with anaemia. 83.5% of patients had normal involution of uterus. 8.8% patients had subinvolution of uterus after delivery [Table 6]. (p value 0.001, chi square 29.47).

Failure of lactation-85.4% patients could initiate breast feeding. 6.8% of patients could not initiate lactation. Significant association was seen between anaemia and non-initiation of lactation (p-value <0.001, chisquare31.53). 38.83% babies were preterm (40 in 103 deliveries). In our study population we had 70 babies with birth weight < 2.5kg (67.96%) and 29 babies with birth weight < 2 kg (28.15%). 21.35% babies had Apgar score < 7 and 22 NEONATAL INTENSIVE CARE UNIT admissions of babies asphyxiated with Apgar score less than equal to 7 (21.35%) (Table:8). 17 patients with intrauterine deaths out of 103 deliveries [Table 7]; i.e. a frequency of 16.5% and Out of 103 patients, 7.8% patients had maternal mortality (p value <0.001, chi square 26.97) which were significantly associated with maternal anaemia.

Table 1: Distribution of study population according to grade of anemia [n-103]					
Anemia Category	Frequency	Percentage			
Mild	4	3.9			
Moderate	56	54.4			

Severe	36	35.0
Very Severe	7	6.8
Total	103	100.0

Table 2: Association of Anemia with Pregnancy-Induced Hypertension						
Pregnancy Induced Hypertension	Mild	Moderate	Severe	Very Severe	Percentage	
Yes	1	16	10	4	30.09	
No	3	40	26	3	69.90	
Total	4	56	36	7	100	

Table 3: Association of Anemia with Post Partum Hemorrhage [n-103]						
Post-Partum Hemorrhage	Mild	Moderate	Severe	Very Severe	Chi square, p value	
Yes	3(12.0)	9(36.0)	10(40.0)	3(12.0)	9.20, 0.027	
No	1(1.4)	47 (60.3)	26(33.3)	4(5.1)		
Total	4	56	36	7		

Table 4: Association of Anemia with Antenatal Infection [n-103]						
Antenatal Infection	Mild	Moderate	Severe	Very Severe	Chi square, p value	
No	4(4.7)	54(62.8)	27(31.4)	1(1.2)	33.80, 0.000	
Yes	0(0.0)	2(11.8)	9(52.9)	6(35.3)		
Total	4	56	36	7		

Table 5: Association of Anemia with Postnatal Infection[n-103]						
Postnatal Infection	Mild	Moderate	Severe	Very Severe	Percentage	
NA	0	1	3	4	7.76%	
Yes	0	15	18	3	34.95%	
No	4	40	15	0	57.28%	
Total	4	56	36	7	100%	

NA- Not Applicable as patients deceased

Table 6: Association of Anemia with Subinvolution of Uterus							
Subinvolution of uterus	Mild	Moderate	Severe	Very Severe	Chi square, p value		
NA	0(0.0)	1(12.5)	3(37.5)	4(50.0)	29.47, 0.001		
No	3(3.5)	51(58.1)	30(34.9)	3(3.5)			
Yes	1(12.5)	4 (50.0)	3(37.5)	0(0.0)			
Total	4	56	36	7			

NA- Not Applicable as patients deceased

Table 7: Association of Anemia with Intrauterine Death						
Intra Uterine Death	Mild	Moderate	Severe	Very Severe	Chi square, p value	
Yes	0(0.0)	4(23.5)	8(47.1)	5(29.4)	20.53, 0.000	
No	4(4.7)	52(60.5)	28(32.6)	2(2.3)		
Total	4	56	36	7		

Table 8: Association of Anemia with NEONATAL INTENSIVE CARE UNIT Admission

Neonatal Intensive Care Unit adm.	Mild	Moderate	Severe	Very Severe	Chi square, p value
Yes	1(4.5)	5 (22.7)	14 (63.6)	2 (9.1)	
No	3 (3.7)	51(63.0)	22(27.2)	5 (6.2)	11.98, 0.007
Total	4	56	36	7	

DISCUSSION

In India, it is common to see patients with anaemia late in pregnancy and in labour with no prior antenatal visits and the same was evident from our present study. This clinical study was done to know the effects of maternal anaemia on mother and fetal outcome. In our cross sectional study, demographics of Severity of anaemia were- Mild anaemia was present in 3.9%, Moderate anaemia was present in 54.4%, Severe anaemia in 35% and Very severe anaemia in 6.8%. This was similar to the study by Viveki et al 22,^[13] and Agarwal et al,^[5] maximum number of patients 251 (79.9%) were moderately anemic, whereas 39 (12.4%) had mild anaemia and only 24 (7.6%) had severe anaemia. 89.33% women were multigravida and 10.67% were primigravida. The present study revealed that anaemia was significantly more common in multigravida women than primigravida which was in concordance with the other studies. In study by Shyama et al [2012],^[14] 41.7% women were primigravida. In another study by Kefiyalew et al [2014],^[15] majority of pregnant anaemic women (80.2%) were multigravida.

Haematinics- The current study showed that 54.4% of patients did not take any iron, folic acid supplements during pregnancy. It was observed that

most women did not come for ANC check-up and some of those who came for the check-up were noncompliant with iron- folic acid tablets (IFA) The COVID19 crisis resulted in an increase in micronutrient malnutrition, including anemia due to the disruption of health services and food systems on top of an economic crisis. Cochrane KM et.al Clinical trial study based on prevalence of iron deficiency anemia and supplementation practices among pregnant women, from 2019 to 2022 suggest the incidence of iron deficiency without anemia may be even higher. Individuals with iron deficiency anemia during pregnancy, when the demand for iron increases.

Postpartum hemorrhage (PPH) It was seen in 24.3% of patients [Table 3]. Association of anaemia with postpartum haemorrhage was significant, p value 0.027, chi square value 9.20.

We found a statistically significant relationship between anemia in pregnancy and postpartum hemorrhage and also the occurrence of postpartum hemorrhage to be higher in moderately and severely anemic mothers compared to those with mild anemia and normal mothers. This result is in line with the findings of Nair et al. who reported that women with severe anemia had nine times higher odds of postpartum hemorrhage.^[17] This was similar to study by Rohilla et al,^[9] POST PARTUM HEMORRHAGE was significantly associated with the varying degree of severity of anaemia. Frass in her observational studies explained the relationship between POST PARTUM HEMORRHAGE and severe anaemia accounting for about 90%.^[8] Kavle found that blood loss at delivery was slightly elevated in mild anaemic women as compared to non anaemic women.^[18] He also observed strong association between the severity of anaemia with blood loss at delivery and in the post-partum period. Anemia in pregnancy is linked to postpartum hemorrhage in terms of uterine atony. The more severe the anemia, the more likely the greater blood loss and adverse outcome. Because anaemia reduces the oxygen-carrying capacity of the blood, anaemic women cannot tolerate the same volume of blood loss as healthy women. In multivariate analysis done, Justine A Kavle et al showed women with moderate-to-severe anaemia at enrollment had a significantly greater total blood loss (91 mL) average compared to non-anaemic women (p<0.01).^[18] Several biological mechanisms are thought to play a role in postpartum haemorrhage. Higher blood loss may be attributed to impaired uterine muscle strength for labor which can be prolonged, or decreased resistance to infection, as infection is suggested to contribute to uterine dysfunction or inertia. Decreased uterine blood flow or low uterine muscle strength may contribute to inefficient uterine contractions and contribute to blood loss, potentially mediated by low body iron stores (serum ferritin <100 µg/L) and, therefore, iron-deficiency anaemia. Severe anemia is

hypothesized to impair tolerance of postpartum haemorrhage and contribute to maternal death, possibly due to the failure of women to endure such excessive blood losses.

In our study, the associations between blood loss and maternal anaemia emanate from women with timely hospital admission, measures taken to correct anemia, measures taken to control blood loss during delivery, and a few occurrences of severe bleeding. These data suggest the influence of maternal anaemia on blood loss at childbirth and postpartum is more pervasive. Our findings are likely to be underestimates of the effect of anaemia on blood loss as the data is collected on women residing in town areas with hospital-based births, rather than home-based deliveries as are common in hilly regions of Uttarakhand where access to healthcare may be limited, and chronic, untreated anaemia is likely to occur.

Antenatal infections were seen in 16.5% [Table 4]. Postnatal infection was present in 36 patients [34.95%] [Table 5]. Significant association was seen between anaemia and infections. (p value <0.001, chi square 33.80) Anaemia depresses the immune status of women and makes them more prone to infections. Wei Sheng Yan Ji. 2006 Jan;35,^[19] determined T lymphocyte subsets level (CD3+, CD4+ and CD8+), nature kill cells activity (CD16), interleukin-2 (IL-2) and serum IgA, IgG, IgM and complement C3 in 3 different women groups, including Iron Deficiency Anemia pregnant women. The level of CD3+ and CD4+ cells, the ratio of CD4+/CD8+ cells, serum IL-2 as well as IgG levels in the anaemic pregnant women were significantly lower than that of those normal pregnant women (P < 0.01, P < 0.05, P < 0.05, P < 0.01). With the decreasing extent of Hemoglobin, these significant immunological indices of pregnant women decrease. The incidence of infectious diseases in Iron Deficiency Anemia pregnant women was significantly higher than that in normal pregnant women (P < 0.05).

Failure of lactation-85.4% patients could initiate breast feeding. 6.8% of patients could not initiate lactation. Significant association was seen between anaemia and non-initiation of lactation. p-value <0.001, chisquare31.53. The study by Feleke et al shows it to be as high as 43%. A study published in NIH, national library of medicine found that anemic mothers reported a higher level of symptomatology associated with insufficient milk and were more frequently classified as having insufficient milk syndrome. Mothers with the syndrome reported a shorter period of full breastfeeding, and weaned at an earlier age.

Subinvolution of uterus-In our study, 83.5% of patients had normal involution of uterus. 8.8% patients had subinvolution of uterus after delivery. P value 0.001, chi square 29.47 [Table 6].

Mortality-We observed maternal mortality of 7.8%. p-value <0.001, chi square 26.97. Anemic mothers do not tolerate blood loss during childbirth; as little as 150 ml can be fatal. Normally, a healthy mother during childbirth may tolerate a blood loss of up to 1000 ml. A review of observational studies showed a linear association between maternal anaemia and death, with each 1.0 g/L increase in maternal haemoglobin associated with a 29% reduction in maternal mortality.^[20] Black RE, Victora CG, Walker SP et al.in their study on Maternal and child undernutrition and overweight in low-income and middle-income countries,^[21] concluded that severe anaemia during pregnancy or post-partum doubled the risk of maternal death. Severe anaemia can lead to circulatory decompensation, increased cardiac output, an increased risk of haemorrhage, and decreased ability to tolerate blood loss, leading to circulatory shock and death.

In Our Study Pregnancy-induced hypertension was present among 31/103 (30.09%) of mothers with anaemia. The susceptibility of women with severe anaemia to preeclampsia could be explained by a deficiency of micronutrients and antioxidants. Recent results indicate that reduction in serum levels of calcium, magnesium and zinc during pregnancy might be possible contributors to the development of preeclampsia.^[23]

Several studies have shown the association between severe anemia and preeclampsia and thus considers anemia as one of the main and treatable risk factor for pre-eclampsia. A prospective study by Poorana Devi (2014),^[22] Showed anemic patients were more prone to develop preeclampsia due to associated hypoproteinemia. More severe the anemia, greater the chance to get preeclampsia.

Fetal outcome-Maternal anemia has been associated with several adverse consequences in birth outcomes such as low birth weight (LBW), preterm birth and small-for-gestation age (SGA), Intrauterine Death, baby being preterm asphyxiated and requiring NEONATAL INTENSIVE CARE UNIT admissions in the immediate postnatal period. In our current study16.5% pregnant patients had Intrauterine Death; 21.35% babies were admitted in NEONATAL INTENSIVE CARE UNIT. These adverse birth outcomes are risk factors for poor cognitive development of children afterbirth. A basic principle of fetal/neonatal iron biology is that iron is prioritized to red blood cells at the expense of other tissues, including brain. When iron supply does not meet iron demand, the fetal brain may be at risk even if the infant is not anemic. Although dietary deficiency may be contributory, the etiology of the vast majority of cases of iron deficiency anemia in infancy and childhood is maternal iron deficiency anemia in pregnancy.

Study on Maternal and Perinatal Morbidity and Mortality Associated with Anemia in Pregnancy done by AU Smith C et al concluded that Anemia was associated with preterm birth, small-forgestational-age live birth, low 5-minute Apgar score, neonatal death, and perinatal death.^[25]

Preterm babies-Ambivalent findings have also been published on the relationship between prenatal anemia and preterm birth (gestational age < 37 weeks).^[38,39] A recent study in India reported a 2.4fold increase in the risk of preterm births among anemic pregnant women compared to non-anemic pregnant women.^[26] Although many researchers have used the clinical threshold of 11.0 g/L to define prenatal anemia, others who have used the Hemoglobin or hematocrit levels or categories of severity of anemia (mild to severe or quantiles of Hemoglobin) have reported a non-linear relationship between prenatal anemia and the risk of some adverse birth outcomes. In our study there were 38.83% [40 in 103 deliveries] preterm babies which is in line with the study by Shweta Kumari, Neelima Garg et al at Jharkhand who found prevalence of 34.75% of preterm babies in anaemic mothers.^[27] However, Qiaoyi Zang, Candi V Ananth, Zhu li et al in their study 1996 had preterm birth prevalence of 4.1%.^[28]

Low birth weight-LBW is defined as birth weight less than 2500 g at term and is an indication of poor fetal growth. Most of the published literature on maternal anemia and LOW BIRTH WEIGHT show irrefutable evidence of the increased risk of LOW BIRTH WEIGHT and SMALL-FOR-GESTATION AGE deliveries, among severely anemic pregnant women even after adjusting for potential confounders. Considering the increased demand for nutrients and oxygen during pregnancy, it is not unlikely to anticipate poor fetal growth for babies of anemic women. In our study population we had 70 babies with birth weight < 2.5 kg [67.96%] and 29 babies with birth weight < 2 kg [28.15%]. However, Shweta Kumari, Neelima Garg et al in their study at Jharkhand had prevalence of 32.81% of low birthweight babies.^[27] In the study by Ram Hari Ghimire et al 2012, had the frequency of Low-Birth-Weight babies as 22% in anaemic patients.^[29] In the study by Koller et al,^[30] the authors observed an inverse relationship between birth weight and Hemoglobin concentration in the late trimester among 113 non-anemic pregnant women with uncomplicated pregnancies. Following the study, in 1983, Murphy et al,^[31] published in the Lancet, a larger study of over 54 000 singleton pregnancies, in which they observed an increased risk of preterm birth, LOW BIRTH WEIGHT and perinatal mortality among pregnant women with Hemoglobin less than 10.4 g/L and those with Hemoglobin greater than 13.2 g/L in the first and second trimesters.^[31] Thus U or V- shaped relationship shows adverse neonatal outcome at extremes of haemoglobin. Using the cut-off of 11.0 g/L to compare the risk of Low Birth Weight in anemic and non-anemic women, Finkelstein et al,^[20] and Ahmad et al reported increased risk of Low Birth Weight among anemic women. Whereas. Demmoucheet al.^[33] and Buzyan.^[32] found no relationship between prenatal anemia and LOW BIRTH WEIGHT. Fetuses with growth restrictions are highly at risk of preterm birth, Low Birth Weight, perinatal morbidity and mortality. Anemia

during pregnancy has often been linked with Low Birth Weight. Our results suggest a significant relationship between maternal anemia and low birth weight; this is comparable with the findings of Parks et al, where severe maternal anemia was associated with low birth weight.^[35]

Neonatal Intensive Care Unit admissions -In the current study we had 22 Neonatal Intensive Care Unit admissions of babies asphyxiated with Apgar score less than equal to 7 (21.35%) [Table 8]. Admission to the neonatal intensive care unit (NICU) was higher among the neonates born to mothers with severe anemia, 15.5% (n =16), as compared to mothers with moderate anemia, 4.8 % (n = 5), and mild anaemic mothers, 0.9% (n = 1), with a statistically significant difference between the groups (p<0.001). Study done on Anemia in Pregnancy by Alexander Muacevic et al- The significant fetal outcomes that were associated with maternal anemia are low birth weight in moderately anemic mothers (22.7%), Neonatal Intensive Care Unit admissions in mildly anemic mothers (12.5%), and the development of congenital malformations (9.7%) in mildly anemic mothers, which indicates an important need to identify the root causes and risk factors that lead to anemia in pregnancy.^[36]

Intrauterine deaths- In our current study we had 17 patients with intrauterine deaths out of 103 deliveries; i.e. a frequency of 16.5% [Table 7]. The study by F. W. Lone et al. Maternal anaemia and perinatal outcome Newborns of anaemic mothers had 1.8 times increased risk of having an APGAR score of <5 at 1 min and the risk of INTRAUTERINE DEATH was 3.7 times higher for anaemic women. They concluded that low maternal haemoglobin levels are associated with increased risk of preterm delivery, LOW BIRTH WEIGHT babies, APGAR score <5 at 1 min and Intrauterine Death.^[37]

CONCLUSION

Maternal anaemia is an increasing cause of INTRAUTERINE DEATH, LOW BIRTH WEIGHT, Preterm delivery and NEONATAL INTENSIVE CARE UNIT admissions. Timely identification of women with maternal anaemia and associated maternal and fetal complications like antenatal infections, postnatal infections, POST PARTUM HEMORRHAGE, PREGNANCY-INDUCED HYPERTENSION, subinvolution of uterus, failure of lactation, preterm, LOW BIRTH WEIGHT. requirement for NEONATAL INTENSIVE CARE UNIT, INTRAUTERINE DEATH and maternal mortality can help in reducing maternal morbidity and mortality.

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