Review

Anemia in Cambodia: prevalence, etiology and research needs

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Anemia is a severe global public health problem with serious consequences for both the human and socio-economic health. This paper presents a situation analysis of the burden of anemia in Cambodia, including a discussion of the country-specific etiologies and future research needs. All available literature on the prevalence and etiology of anemia in Cambodia was collected using standard search protocols. Prevalence data was readily identified for pre-school aged children and women of reproductive age, but there is a dearth of information for school-aged children, men and the elderly. Despite progress in nation-wide programming over the past decade, anemia remains a significant public health problem in Cambodia, especially for women and children. Anemia is a multi-faceted disease and both nutritional and non-nutritional etiologies were identified, with iron deficiency accounting for the majority of the burden of disease. The current study highlights the need for a national nutrition survey, including collection of data on the iron status and prevalence of anemia in all population groups. It is impossible to develop effective intervention programs without a clear picture of the burden and cause of disease in the country.

Key Words: anemia, Cambodia, etiology, prevalence, hemoglobin

INTRODUCTION

Anemia is a global public health problem, with major consequences for human health and socio-economic development. According to a review of nationally representative survey data from 1993-2005, the World Health Organization (WHO) estimates that more than 1.62 billion people are affected by anemia.[1] The condition is inherently associated with poverty and is therefore particularly prevalent in the developing world where the problem is often exacerbated by limited access to appropriate healthcare and treatment options.[2] Anemia occurs at all stages of life, but is particularly prevalent in women of reproductive age, pregnant women and children.

Anemia is characterized by a decrease in the normal number of red blood cells or less than the normal quantity of hemoglobin in the blood.[3] The condition is determined by the expected normal range of hemoglobin in a population, and is defined as existing in an individual whose hemoglobin concentration (Hb) has fallen below a threshold lying at two standard deviations below the median for a healthy population with the same demographic characteristics, including age, sex and pregnancy status.[1] Specific cut-off values of hemoglobin for various demographic groups for determining the presence of anemia have been established by the WHO (Table 1).

The etiology of anemia is multifaceted and often several factors are at play in an anemic individual. Nutritional anemia as a result of iron deficiency is the most common cause of anemia worldwide: approximately 50-60% of all cases of anemia are attributed to a lack of iron in the diet.[1,3] Additionally, other micronutrient deficiencies, some infectious diseases, genetically-determined hemoglobin-opathies, and chronic or acute blood loss are also known to cause anemia.[4]

The consequences of anemia can be quite severe and are often irreversible, affecting both human and socio-economic health of individuals and families. Mild to moderate anemia leads to weakened immunity, reduced work capacity, reduced cognitive ability and an overall decreased quality of life.[3,5] Severe anemia (Hb <70g/L) reduces a woman's ability to survive bleeding during and after childbirth and is considered a major cause of maternal morbidity and mortality, particularly in the non-industrialized world.[6] Anemia during pregnancy is also associated with increased risk of premature delivery and low birth-weight, resulting in an increase in perinatal mortality.[6] Delayed cognitive development and limitation in intellectual development is also a major concern in children and adolescents.[4]

The objective of this paper is to present a situation analysis of the burden of anemia in Cambodia. Drawing upon available information; prevalence estimates will be examined by demographic sub-populations and trends will be briefly discussed. The data presented are not all

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Table 1. Hemoglobin levels (g/L), below which anemia is present in a person by age, gender and pregnancy status.[2]

	Subgroup	Hemoglobin concentration (g/L)
Children	6-59 months	110
	5-11 years	115
	12-14 years	120
Women	Non-pregnant >15 years	120
	Pregnant	110
Men	>15 years	130

based on representative national sampling; rather, the paper utilizes data from reports, publications and reviews that are readily available. The second section will discuss both general and country-specific etiologies of anemia, including nutritional and non-nutritional factors.

SITUATION ASSESSMENT AND ANALYSIS

In order to estimate the burden of anemia in Cambodia, a literature search was performed to find all available research which examined the condition in the general population and/or specific sub-populations. The search was performed digitally, using PubMed and Google Scholar, with the various combinations of the key words "anemia" or "anaemia", "iron deficiency", "nutrition" in addition to "Cambodia" and/or "South East Asia". In addition, a search of the WHO Vitamin and Mineral Nutrition Information System, Government of Cambodia online databases and reports, and reports from non-governmental organizations was performed by both manual search, and keyword search as above. Finally, the Government of Cambodia maintains a food security and nutrition website that includes a document library which was also manually searched. All available white and grey literature was first screened for relevance, and included only if the method of detection and a clear description of the study population were provided.

To date, there has not been a comprehensive, nationally-representative nutrition survey focusing on both macro- and micronutrients across all demographic groups and in both men and women conducted in Cambodia. Data on the prevalence of anemia, however, can be drawn from three internationally sponsored and facilitated Cambodian Demographic and Health Surveys (CDHS) conducted in 2000, 2005 and 2010. These surveys are considered to be nationally representative and involved more than 15,300, 16,800, and 18,750 women aged 15 – 49 in 2000, 2005, and 2010 respectively.[7-9] To add context to these survey results, the prevalence of anemia by age group is compared over time using chi-square tests.

Anemia prevalence data can also be taken from individual studies that have been conducted in Cambodia to investigate various treatments for anemia and/or to study the prevalence of anemia in specific population groups. These studies are not nationally representative and there is a strong focus on the extent of the problem in rural areas of the country. Regardless, this information is valuable in indicating the magnitude of the problem. Where possible, data has been presented according to urban/rural status, the study setting, age, sample size of the specific study, and method of diagnosis; sampling methodology varied by study and is listed in Tables 2-4.

Infants and Pre-School Children

The largest body of data on the prevalence of anemia in Cambodia has been collected on this high-risk demographic. The three Cambodian Demographic Health Surveys (CDHS) and several additional intervention studies provide prevalence data, with anemia present at hemoglobin levels <110 g/L (Table 2). The CDHS conducted in 2000 indicated a prevalence of 57.3% and 64.4% of anemia in children aged 0.50–4.99 years in urban and rural Cambodia, respectively.[7] Using Chi-square analysis, these prevalence estimates were not found to differ significantly in 2005: 59.7% of children from urban populations (p=0.54) and 62.2% of children from rural areas (p=0.67) were found to be anemic.[8] In 2010, 44.7% of urban and 56.9% of rural children were anemic, representing significant prevalence reductions from both 2005 and 2000 (p<0.001).[9] In addition to these national surveys, prevalence estimates from various studies suggest that anemia affects between 54.0–82.0% of infants and pre-school children in the country.[4,10-16]

School-aged children and Adolescents

Unfortunately, high quality data on the prevalence of anemia in school-aged children in Cambodia is limited (Table 3). Longfils and colleagues estimated that the prevalence of anemia was 64.1% among grade-one students at two primary schools in rural Kampot province, using a sample size of 450.[17] The ages of these students ranged from approximately 6 to 15 years, thus this study provides important data on the prevalence of anemia across a wide age-range.

McLean reported 21.2% prevalence of anemia in 231 girls enrolled in secondary school, ranging from 9-21 years of age.[18] This estimate was lower than anticipated by the authors, and these results must be interpreted cautiously. In Cambodia, only about 25% of girls attend secondary school,[8] and those that do are typically of higher socioeconomic status and are therefore more likely have a diet that is higher in heme iron when compared to those who are less affluent. Future surveying efforts should focus on collection of data from both adolescents who are and who are not attending secondary school, representing the full range of socioeconomic statuses in a weighted representative sample.

One final intervention study included baseline measurement of anemia caused specifically by iron deficiency.[19] In Kampot Province, 805 students from a secondary school, and 699 students from a primary school were assessed for hemoglobin and iron status. Prevalence of iron deficiency anemia was approximately 7% and 13% in the secondary and primary schools, respectively. The primary school selected for this study was, prior to the trial, part of a school feeding program run by the World Food Programme and this may partly account for the low prevalence of iron deficiency anemia reported.

Adult Females

The reproductive status of women is an important factor

Table 2. Summary of prevalence data on anemia among pre-school children in Cambodia

Reference	Area	Place	Setting	Study period	Age group	Count	Sampling design	Hb method	Prevalence of anemia (severe)
CDHS 2010[9]	U	National	Com.	2010	0.50-4.99	548	2-stage cluster sampling within U/R strata	HemoCue	44.7 (0.5)
CDHS 2010[9]	R	National	Com.	2010	0.50-4.99	3129	2-stage cluster sampling within U/R strata	HemoCue	56.9 (0.9)
CDHS 2010[9]						3677			55.1 (0.9)
CDHS 2005[8]	U	National	Com.	2005	0.50-4.99	400	2-stage cluster sampling within U/R strata	HemoCue	59.7 (0.6)
CDHS 2005[8]	R	National	Com.	2005	0.50-4.99	2758	2-stage cluster sampling within U/R strata	HemoCue	62.2 (0.7)
CDHS 2005[8]						3158			Total: 61.9 (0.7)
CDHS 2000[7]	U	National	Com.	2000	0.50-4.99	196	2-stage cluster sampling within U/R strata	HemoCue	57.30 (2.3)
CDHS 2000[7]	R	National	Com.	2000	0.50-4.99	1265	2-stage cluster sampling within U/R strata	HemoCue	64.4 (2.0)
CDHS 2000[7]						1461			63.4 (2.0)
Kenfick 1998[9]	R/U	125 villages	Com	1998	0.50-4.99	1348	Multistage random sampling	HemoCue	82.0 (2.8)
Kenfick 2000[10]	R/U	137 villages	Com	2000	0.50-4.99	1588	Multistage random sampling	HemoCue	74.0
HKI 2000[11]	R	10 rural provinces	Com	2000	0.50-4.99	1762	Random multistage cluster sampling	HemoCue	54.0
Johnston 2003[4]	R/U	124 villages	Com	2003	0.50-4.99	1341	Two-stage random sampling	HemoCue	72.15 (1.6)
Giovannini 2006[12]	R	1 district, 24 villages	Com	2003	0.50 +/- 7 days	204	Two-stage random sampling	CBC (CellDyn 3200)	78.8
Schumann 2009[13]	R	1 province, 13 villages	Com	2003	0.50-2.00	250	Two-stage random sampling	CBC (CellDyn 3200)	74.4
Helmers 1999[14]	R	40 villages, 20 communes	Com	1999	0.50-4.99	1005	Two-stage random sampling	HemoCue	67.0 (3.3)
Talukder 2010[15]	R	Not available	Com	2005	0.50-4.99	~ 125	Two-stage random sampling	HemoCue	76.0

Abbreviations: U, urban; R, rural; Com, Community-based

when considering the prevalence of anemia. Pregnant and lactating women have a higher demand for nutritional sources of iron in order to maintain normal hemoglobin levels because they require an adequate iron supply for the growth of the foetus and/or the production of milk.[3] For this reason, it is beneficial to categorize women as non-pregnant and non-lactating (NPNL), pregnant (PW), lactating (LW), and/or pregnant or lactating (PWLW) (Table 4).

The CDHS conducted in 2000 estimated a 55.1% and 66.3% prevalence of anemia in NPNL (Hb <120 g/L) and PWLW (Hb <110 g/L), respectively.[7] The prevalence estimates decreased significantly (p <0.001) five years later with anemic NPNL women representing 44.3% of the population, and 55.4% of PWLW estimated to be anemic.[8] In 2010, 43.4% of NPNL women were anemic, and 49.9% of PWLW, signifying a further reduction in

the overall prevalence.[9]

Additional, non-nationally representative studies report a wide range in the reported prevalence of anemia. Estimates suggest that 61.0%-69.0% of non-pregnant women and 72.0%-77.0% pregnant women are anemic.[10,11,15] Two studies with much smaller sample sizes did not separate according to reproductive status, and estimate 25.0%-33.0% prevalence of anemia in all women surveyed.[18,20]

Summary of the situation analysis
The lack of data presented herein highlights the need for a comprehensive national nutrition survey including measurement of micronutrient, but also macro-nutrient status, among all ages in both genders. There is a relative abundance of data on infants and preschool-aged children, and this is an important group to monitor as effects of anemia can be most severe during these important developmental

Table 3. Summary of prevalence data on anemia among school-aged children in Cambodia

Reference	Area	Place	Setting	Study period	Age group	N	Sampling design	Hb method	Prevalence of anemia (severe)
Longfils 2008[16]	R	2 villages, 2 districts	2 primary schools	1999	Grade 1 children (6-15 years)	451	All grade 1 children present on sampling day	Lovibond method	64.1
McLean 2009[17]	R	4 provinces	32 secondary schools	2007-2008	9-21 years	231	Random multi-stage cluster sampling	CBC (Sysmex KX21)	21.2
Longfils 2008[18]	R	1 province	1 secondary school	2005	6-21 years	805	2-stage sampling; purposive sampling to include students with IDA	CBC (CellDyn 3200)	7%[†]
Longfils 2008[18]	R	1 province	1 primary school	2005	6-21 years	699	2-stage sampling; purposive sampling to include students with IDA	CBC (CellDyn 3200)	13%[†]

Abbreviations: U, urban; R, rural; IDA, iron-deficiency anemia; N, sample size
[†] Prevalence of IDA

years. Iron requirements are increased during periods of marked growth, including puberty; therefore the lack of data on the prevalence of anemia in school-aged children and adolescents is a concern. Quite obvious is the complete absence of data on the prevalence of anemia in men. Anemia is often considered a disease of women and children, but men are also at risk and nationally representative data for this group should be collected. Similarly, data on the prevalence of anemia in the elderly is absent, with the majority of surveys setting an upper age limit for inclusion of 50 years. Given that the quantity and quality of diet typically decreases with age,[21] there is likely to be a high prevalence of anemia in older individuals that is not captured by the current research.

Overall, the three nationally-representative health surveys show that the prevalence of anemia remained unchanged in children aged 0.50-4.99 years. Fortunately, in women of reproductive age, anemia prevalence dropped approximately 11 percentage points for both NPNL and PWLW between 2000 and 2005.[7-9] Despite this progress, the prevalence of anemia in these groups remains unacceptable and continues to present a severe public health problem according to WHO standards.[3]

ETIOLOGY OF ANEMIA
Anemia is the result of a wide variety of causes that can be isolated, but more typically co-exist. Commonly, anemia results from dietary iron deficiency, which is a major cause of anemia worldwide.[1] Non-nutritional causes of anemia are numerous and diverse. In the developing world, common infections which may be both chronic and recurrent are associated with blood loss that can result in iron deficiency and ultimately anemia. In addition, inherited abnormal hemoglobin traits, acute haemorrhage and various chronic diseases are also contributing factors.

i) Iron deficiency anemia
Iron status can be considered as a continuum from iron deficiency with anemia (IDA), to iron deficiency without anemia, to normal iron status, and finally to iron overload. The WHO estimates that approximately 50% of all anemias can be attributed to iron deficiency.[1]

Iron deficiency anemia may result from a single, or any combination of four major factors: i) inadequate daily iron intake and/or iron bioavailability; ii) increased iron needs at various stages of life, including pregnant women, children and adolescents; iii) chronic iron loss due to menstruation, ulcers or parasitic infection; and, iv) impaired iron utilization after absorption as a result of repeated infection and/or concomitant micronutrient deficiencies.[3]

In Cambodia, data are scant on the prevalence of IDA and inference from surveys on the prevalence of general anemia must be used. To determine the prevalence of iron deficiency, hemoglobin concentration plus an indicator of iron status, most commonly serum ferritin, must be examined.[3,22] Hemoglobin is easily measured with a capillary blood sample using a portable hemoglobin monitor, such as the HemoCue® system (HemoCue AB, Ängelholm, Sweden), but serum ferritin analysis requires a venous blood sample. Serum ferritin is an acute-phase protein that is elevated in response to infectious disease or inflammatory processes, and this must be taken into account when conducting an analysis of this data.[3] For this reason, the majority of research on the prevalence of anemia in the developing world, including Cambodia, provides only hemoglobin data and the prevalence of IDA can therefore only be estimated.

Trend analysis from the three, nationally-representative Demographic and Health Surveys showed that the prevalence of anemia in children was highest in the 6 to 24 months age category, but that the situation eventually improves after 2 years of age (Figure 1).[7,8,9] This markedly high prevalence of anemia in pre-school aged children coincides with a child's peak period of growth when iron requirements would be elevated; thereby suggesting that iron deficiency is a significant cause of anemia in this age group.[4]

Three intervention studies reported above also included markers of iron deficiency and the prevalence of iron deficiency and/or IDA can therefore be calculated. In 2009, Schumann *et al*. conducted a study on the efficacy of iron supplements in 250 rural children. At baseline, iron deficiency was estimated to be present in 44.0% of children

Table 4. Summary of prevalence data on anemia among women in Cambodia

Reference	Area	Place	Setting	Study period	Status	Age group	Count	Sampling design	Hb method	Prevalence of anemia (severe)
CDHS 2010[9]	R/U	National	Com	2010	NPNLW	15.00-49.99	7385	2-stage cluster sampling within U/R strata	HemoCue	43.4 (0.4)
CDHS 2010[9]	R/U	National	Com	2010	PW	15.00-49.99	469	2-stage cluster sampling within U/R strata	HemoCue	52.7 (0.0)
CDHS 2010[9]	R/U	National	Com	2010	LW	15.00-49.99	1376	2-stage cluster sampling within U/R strata	HemoCue	47.1 (0.0)
CDHS 2010[9]							9229			Total: 44.4 (0.4)
CDHS 2005[8]	R/U	National	Com	2005	NPNLW	15.00-49.99	6408	2-stage cluster sampling within U/R strata	HemoCue	44.3 (0.9)
CDHS 2005[8]	R/U	National	Com	2005	LW	15.00-49.99	486	2-stage cluster sampling within U/R strata	HemoCue	57.1 (3.4)
CDHS 2005[8]	R/U	National	Com	2005	PW	15.00-49.99	1325	2-stage cluster sampling within U/R strata	HemoCue	53.6 (0.8)
CDHS 2005[8]							8219			Total: 46.6 (1.0)
CDHS 2000[7]	R/U	National	Com	2000	NPNLW	15.00-49.99	2722	2-stage cluster sampling within U/R strata	HemoCue	55.1 (0.7)
CDHS 2000[7]	R/U	National	Com	2000	PW	15.00-49.99	209	2-stage cluster sampling within U/R strata	HemoCue	66.4 (4.3)
CDHS 2000[7]	R/U	National	Com	2000	LW	15.00-49.99	680	2-stage cluster sampling within U/R strata	HemoCue	66.1 (2.6)
CDHS 2000[7]							3634			Total: 57.8 (1.3)
Charles 2011[19]	R	1 district	Com	2008	All women	20.0-74.0	120	2-stage random sampling	CBC (CellDyn 3200)	25.0
Helmers 1999[14]	R	40 villages, 20 communes	Com	1999	NPW	N/A	924	2-stage random sampling	HemoCue	69.0
Helmers 1999[14]	R	40 villages, 20 communes	Com	1999	PW	N/A	112	2-stage random sampling	HemoCue	72.0
Kenfick 1998[9]	R/U	125 villages	Com	1998	NPW	N/A	994	Multistage random sampling	HemoCue	69.0
Kenfick 1998[9]	R/U	125 villages	Com	1998	PW	N/A	97	Multistage random sampling	HemoCue	74.0
Kenfick 2000[10]	R/U	137 villages	Com	2000	NPW	N/A	998	Multistage random sampling	HemoCue	61.0
Kenfick 2000[10]	R/U	137 villages	Com	2000	PW	N/A	116	Multistage random sampling	HemoCue	77.0
McLean 2009[17]	R	1 district	Com	2007-2008	WRA	15.0 – 54.0	231	2-stage random sampling	CBC (Sysmex KX21)	33.3

Abbreviations: U, urban; R, rural; Com, community-based; NPNLW= non-pregnant, non-lactating women; NPW=non-pregnant women; PW= pregnant women; WRA=women of reproductive age; N/A=not available; N = sample size

aged 6-24, even when controlling for inflammation.[14]

A 2006 study involving 204 children selected from a single district in Kompong Chhnang province showed that iron deficiency was prevalent in 13.2% of children aged 6 months.[13] However, by 18 months, more than 50% of children in the placebo group (n=62) were reported to be iron deficient, even when accounting for inflammation.

In order to determine the effectiveness of a supplementation program involving 60,000 school girls in five target provinces and 33,000 women of reproductive age in one operational district, McLean surveyed a subsample of the school girls (n=231) and women of reproductive age (n=231) for indicators of iron status.[18] Iron deficiencies were found at baseline in 18.2% of school girls, with IDA affecting 10.4% of participants. In women of reproductive age, iron deficiency and IDA were estimated to affect 19.9% and 12.6% of survey participants, respectively. Following intervention with oral iron supplements, iron deficiency decreased significantly among anemic and non-anemic women at baseline but the proportion of anemia remained unchanged. These findings suggest that iron deficiency was only partially responsible for cases
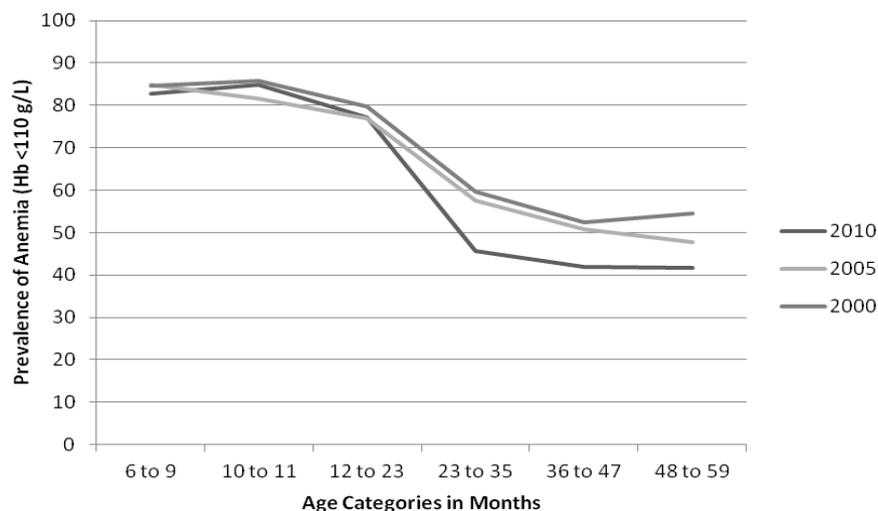
Figure 1. Prevalence of anemia in pre-school aged children (6-59 months) measured in 2000, 2005 and 2010 as part of the Cambodian Demographic Health Survey series.[7-9]

of anemia in the study group, and that various other etiological factors may be at play.[18] Future surveying efforts should assess iron status of the population in order to determine the contribution of iron deficiency to the prevalence of anemia that is currently reported.

ii) Vitamin A and other micronutrient deficiencies
Deficiencies of several key micronutrients may also lead indirectly to anemia, typically by influencing hemoglobin metabolism. These include vitamin A, folate, vitamin B-12, vitamin C, protein, and copper.[23] Vitamin A deficiency, in particular, is a well-established contributor to anemia and is also common in the developing world where dietary diversity is limited.[22] Vitamin A is essential for hematopoiesis, and it is thought that this vitamin is required for the mobilization of iron for hemoglobin synthesis.[24,25]

Data on the prevalence of vitamin A deficiency can be taken from the Demographic and Health Surveys. In 2000, 22% of rural children aged 6-59 months had severe vitamin A deficiency as assessed by serum retinol levels.[7] In 2000 and 2005, only one in three children received a vitamin A supplement within 6 months before the survey.[7,8] In 2010, nearly 71% of children had received vitamin A supplements in the past 6 months, largely attributable to the efforts of the National Vitamin A Policy that was developed in 2009.[9]

In addition to the recent scale-up of vitamin A supplementation, children may also consume dietary vitamin A. The 2005 and 2010 nation-wide surveys collected data on the consumption of vitamin A-rich foods during the 24-hour period prior to surveying.[8,9] Foods rich in vitamin A were consumed by 87.3% of last-born children in the 24-hour period before the survey in 2005, and by 81.8% of the children in 2010. Among women aged 15-49 with a child under three years living with them, 98.5% consumed vitamin A-rich foods in 2005, though this data was not collected in 2010. In 2010, approximately 43% of women received post-partum supplementation with vitamin A. In spite of the progress in scaling-up of vitamin A supplementation programs, especially for children, data

has still not been collected on the total daily vitamin A intake across all demographic subgroups, so it is not possible to determine whether or not daily vitamin A requirements are being met.

iii) Helminths
Helminths are a division of eukaryotic parasites that live inside their host, commonly in the intestinal tract. The organisms can disrupt nutrient absorption leading to weakness and disease and may contribute to anemia by causing blood loss and depletion of iron stores and/or by inhibiting vitamin A absorption; diarrhoea and chronic inflammation are also common side effects.[26] In Cambodia, helminths constitute a major health problem.[27] A survey of intestinal parasite infection in 251 primary school children in Kompong Cham Province was conducted in 2002 and reported an infection prevalence of 57% in males and 51% in females.[28] In a similar survey of 623 schoolchildren in Battambang province,25.7% individuals were infected.[29] Hookworm (*N. americanus, A. duodenale*), whipworm (*T. trichuria*), roundworm (*A. lumbricodes*), *Opisthorchis sp.* and *Echinostoma sp.* were identified, and multiple infections were noted in a subsample of the cases.[4,28,29]

In 2009, the National Nutrition Program developed a policy for widespread deworming of children aged 12-59 months, together with vitamin A supplementation. The most recent estimates show that 56.7% of children received deworming medication in the past 6 months.[9] In contrast, only 25.7% of children received similar deworming medication in 2005.[8] The impact of this program to date may partially explain the decreased prevalence of anemia in children.

iv) Malaria
The world over, malaria is an important cause of anemia as the parasitic infection ultimately leads to hemolysis of red blood cells and a decrease in hemoglobin production. Since 1991, the Cambodia National Malaria Centre is responsible for monitoring the prevalence of malaria in the country.[4] Though malaria was once considered a sig-

nificant cause of morbidity and mortality in Cambodia,[30,31] a high level of deforestation has occurred over the past two decades (29% of primary tropical forest between 2000 and 2005) and this has dramatically decreased the size of suitable habitat for malaria-infected mosquitoes.[32] In turn, the Cambodian Ministry of Health report that the prevalence of malaria has dropped significantly.[4]

In 2009, approximately 64,000 confirmed cases of malaria were reported, with the majority caused by the *Plasmodium falciparum* species of the malaria parasite.[33] Cases appear to be concentrated in rural areas, with a particular clustering along the western border of the country.[30,31] Though malaria may be a contributing factor, the relatively low prevalence and marked clustering in isolated areas of the country suggest that malaria is not a significant cause of anemia in Cambodia.

v) Hemoglobinopathies

Hemoglobinopathies have been widely reported throughout much of Southeast Asia.[34] These conditions are genetically inherited defects that result in abnormal structure of one of the globin chains of the hemoglobin molecule, ultimately leading to anemia.[35] In Cambodia, no nationally representative data is available and future surveying efforts should address this deficiency of data, including the prevalence of co-existent hemoglobinopathies.

Three studies on the prevalence of hemoglobinopathies in specific subpopulations were identified: a study involving 322 urban children aged 6 to 36 months from a single district in Phnom Penh,[36] a population-based sample of 250 children aged 6 to 24 months,[13] and a hospital study involving 260 patients from the Angkor Children's Hospital in Siem Reap province.[34] The prevalence of any, non type-specific hemoglobinopathy ranged from 29.0% to 51.5% in children aged 6 months to 16 years of age.[14,34,36]

Data on the specific type of hemoglobinopathy is yet more limited. Abnormal hemoglobin variant E was found in all three studies, with prevalence of 28.8 – 32.0%;[14,34,36] further analysis in one study revealed that heterozygous variant type E was found in 22.0%, while homozygous variant type E accounted for the remaining cases.[36] Thalassemia was identified in the children's hospital study only, with 35.4% and 0.8% prevalence of α-thalassemia and β-thalassemia, respectively.[34] Despite this high prevalence, the majority of hemoglobinopathies were mild and not clinically significant and may not pose a major health burden in Cambodia, although are likely to be a contributing cause. The infant mortality rate in Cambodia is quite high, and the possibility exists that some children with clinically significant inherited hemoglobin disorders may have failed to survive, resulting in an underestimation.[34]

vi) Others

Several other diverse factors can also cause anemia. Chronic blood loss, from peptic ulcers for example, can be a contributing factor to IDA, though prevalence data in Cambodia has not been collected.[5] Trauma, resulting in acute blood loss, may also induce iron deficiency and IDA dependent upon the severity of haemorrhage.[5] Finally, complications during pregnancy and/or childbirth can result in anemia. In rural Cambodia, approximately 51% of women deliver at home and 33% of deliveries take place in the absence of a trained health professional, thus obstetric haemorrhage may be a major cause of anemia.[9]

IRON INTAKE IN CAMBODIA
i) Dietary Iron Intake

Given that approximately 50% of all anemia may be attributed to iron deficiency, it is imperative to examine iron intake and overall diet composition. The 2005 and 2010 CDHS surveys, along with the 2008 Anthropometric survey, provide limited, nationally-representative data on the consumption of iron-rich foods by women and children.[8,9,37]

The period of birth to two years of age is a critical period for child development, and adequate nutrition is important for optimal growth and health. The most recent nation-wide data suggests that 75.8% of children consume foods rich in iron, with some differences by background characteristics.[9] When compared to 2005 survey data, there is an 11.5% reduction in the consumption of iron-rich foods, though the reason for this is not clear.[8] No gender difference was reported in either survey, however children living in urban areas and those still breastfeeding may have a lower intake of iron-rich foods.

Adequate iron intake is also important for pregnant women and women of reproductive age. Women aged 15-49 with a child under three years living with them were also surveyed for iron intake in 2005 and 2010. Approximately 98% of women reported consuming foods rich in iron during the 24-hour period prior to the survey; these foods include meat (including organ meat), fish, poultry and eggs; this information was not presented in 2010 report.[8,9]

The 2008 Cambodian Anthropometric Survey included a nationally representative sample of 7,495 households with children aged 0 to 59 months.[37] Information on food consumption was collected for both children and mothers, including the consumption of iron-rich foods in the day or night preceding the interview. Organ meats were consumed by 5.8% of children and 7.3% of mothers, flesh meats were consumed by 36.5% of children and 46.1% of mothers, and fish was found to be the most commonly eaten iron-rich food, with consumption reported in 67.3% and 83.9% of children and mothers, respectively.

These values for both women and children only provide data on the consumption of iron rich foods, not whether or not daily iron requirements are met by the diet. Anderson and colleagues reported an adequate intake of iron for non-breastfed toddlers aged 12-36 months, but an inadequate intake for those toddlers who were partially breastfed. However, this data cannot be considered nationally representative and was based on a sample of stunted children from some of the poorest families of Phnom Penh and were therefore more likely to be at risk of suboptimal micronutrient status.[36]

Typical overall meal composition, including consumption of iron-rich foods, but also consumption of enhancers and/or inhibitors of iron absorption should be investigated. Given that the majority of women in Cambodia lack access to iron-fortified food products and other sources of highly bioavailable iron, this group should be considered

a priority for effective intervention programming. Additionally, there is a need for research on the types of iron-rich foods available in Cambodia, including seasonality, cost, and access across the various geographic regions and demographic groups.

ii) Iron Supplementation

Supplementation with oral iron tablets also contributes to overall iron intake. Until recently, Cambodia did not have a preventive iron supplementation program for children, despite anemia being documented as a severe public health problem in this group. For this reason, households needed to purchase iron supplements out-of-pocket and preventive supplementation was therefore quite rare.[7,8]

In 2009, the first-ever National Nutrition Strategy was developed in an effort to combat the burden of disease related to malnutrition and micronutrient deficiency.[38] Currently, research is being conducted in high-risk provinces on the use of multiple micronutrient sprinkles as in-home fortification for children under 2 years of age.[38]The results from the research program are not yet available, though if sprinkles are found to be acceptable and effective, the burden of anemia in children may be greatly reduced.

The use of iron supplements among women aged 15-49 is more widely documented. The 2005 CDHS collected limited data on the intake of and access to micronutrient supplements. Among women aged 15-49 with a child under three years living with them, 17.6% of women took the recommended number (90+ tablets) of iron/ folic acid supplements during their most recent pregnancy.[8] Some women (9.0%) took 60-90 tablets, while 30.8% reported taking fewer than 60 tablets. Importantly, many women (36.8%) did not take iron/folic acid supplements at all during their most recent pregnancy.

In 2010, there has been improvement in both access to, and use of, iron supplements.[9] Nearly 60% of women reported taking 90+ iron tablets (or doses of syrup) during their most recent pregnancy, while 10.4% used no supplementation at all. In addition, 44.9% of women reported use of post-partum iron/folate supplements.

Despite this progress, it is still apparent that many women are either not receiving the recommended number of iron supplements during pregnancy, or they are choosing not to use them even when they do have access. According to the National Guidelines for Iron and Folic Acid Supplementation established in 2007, pregnant and post-partum women should have access to at least 90 fully-funded iron/folic acid tablets during each pregnancy.[39] Distribution is expected to occur at hospitals, health centres and/or through outreach activities where available. Access to supplements appears to be limited by problems with outreach staffing, limited community mobilization for attending outreach activities, inadequate interest and/or poor knowledge about anemia on the receiving side, and/or stock-outs of tablets.[4] The effectiveness of this program, including a more detailed investigation of why nearly 50% of women are not taking the recommended number of iron supplements, must be assessed through continued efforts at nation-wide surveillance in order to better undestnad the effects of intervention programs.

DISCUSSION

This paper reviews the available data on the magnitude and country-specific etiology of anemia in the Cambodian context. Anemia represents a severe public health problem for women and children in Cambodia, with serious consequences for human health and well-being. Available data on the etiology of anemia in Cambodia points to iron deficiency as an important cause of anemia, and this is in keeping with global trends.[1] Other nutritional disorders, such as vitamin A deficiency, hemoglobinopathies, helminths, malaria, and other non-nutritional factors likely contribute to the overall prevalence. Research on the etiology of anemia in Cambodia is needed to clarify the primary causes within the population as it is impossible to design effective treatment and prevention programmes without decisive etiological data in-hand.

This review highlights the need for a comprehensive, nationally representative nutrition survey that elicits data on both the macro- and micro-nutrient status (including iron status) across age groups, for both men and women. Currently, there is dearth of data for a large portion of the population. In particular, there is a complete lack of data on the prevalence of anemia in men and the elderly of both genders, and only a handful of studies, one of which was conducted in a narrow socio-economic bracket, provided information on the situation for school-aged children.

In 2004, the Copenhagen Consensus brought together an international panel of development economists to consider and confront the ten most pressing challenges to global welfare, including human and environmental health.[40] Micronutrient interventions, including iron fortification, ranked at the top of the list and were deemed to be the greatest priority with the highest benefit:cost ratio of any development intervention.[40] These findings were confirmed in 2008, at the most recent Consensus meeting, where iron and zinc fortification were placed within the top three global challenges.[41] This prioritization of iron and other micronutrient interventions emphasizes the need for well-designed, sustainable and effective programming efforts to combat iron deficiency anemia, and related deficiencies in Cambodia and beyond. There is no denying that iron supplementation should be an important component of policies aimed at reducing anemia, but there is also a need for more sustainable solutions. These alternative approaches fall into four broad categories:[42] i) strategies to increase the production of micronutrient rich foods such as programs to improve home production of fruits and vegetables, aquaculture and livestock production; ii) strategies to increase the intake of micronutrient rich foods, including nutrition education to guide consumer food practices and the incorporation of iron into otherwise deficient diets through the use of adventitious iron sources, including iron cookware;[20,43] iii) strategies to increase the bioavailability of micronutrients using home processing techniques (such as fermentation and germination), food-to-food fortification, and proper food preservation; and finally, iv) through the adoption of selectively-bred plants that are designed to increase iron content and bioavailability of staple grains, including rice.

The International Nutritional Anemia Consultative Group (INACG) further recommends the use of an array

of interventions to prevent and correct iron deficiency anemia, and suggest that supplements should only be viewed as one of several tools in reducing the burden of disease.[44] Recent recommendations suggest that only if the amount of absorbable iron in the diet cannot be immediately improved should iron tablets be necessary, as is usually the case with children 6-24 months and pregnant women.[44] The report highlights the possibilities for and effectiveness of various food-based interventions including many of those which are described above. Research in Cambodia must be conducted in order to determine the feasibility and efficacy of these alternative approaches.

Any approach in the treatment and prevention of anemia must consider the multi-factorial nature of the condition. Although iron deficiency is one of the most prevalent etiologies, other contributing factors may require different approaches. Thus a holistic approach to combating anemia should include helminth control, malarial prophylaxis, and provision of safe and affordable reproductive health services to limit blood loss during pregnancy and childbirth, as highlighted in the INACG report.[44] Programming must also target whole families rather than pregnant women and pre-school aged children, alone.

More recently, the National Nutrition Strategy established the goal of provision of micronutrient supplements, including iron, zinc and vitamin A to children in the form of multiple micronutrient sprinkles.[38] This goal of widespread micronutrient intervention, together with deworming and the reduction of protein-energy malnutrition for women and children, represent an important step forward in the health and well-being of the country. Although the effectiveness of the program has not yet been assessed, these are important demographic group that may suffer irreversible functional consequences as a result of anemia, and the strategy must therefore be monitored closely and respond to accordingly.

The adverse effects of anemia on mortality, morbidity and development are abundantly clear. Anemia affects how individuals participate in all areas of life, including work, school and social activities, and this limits the ability to generate income and afford iron-rich sources of food, medical treatment, and school fees. In turn, this leads to constrained social and economic development, ultimately contributing to a viscous cycle of poverty that is difficult to overcome. The overall magnitude of the problem in Cambodia is therefore cause for great concern and an immediate, sustained and holistic intervention is needed. Long-term measures, including food fortification and production programmes, should be adopted and developed in Cambodia to ensure that all demographic groups can benefit from improved iron intake.

The effectiveness of short-term programs targeted at high risk groups must also be further investigated to ensure universal access to and importantly, the use of, iron supplements in both urban and rural areas. In addition, reasons for inadequate availability and/or use of postpartum iron supplements should be considered. The development and implementation of nutrition education campaigns should be considered as a means of disseminating 'best practices' guidelines to the general population, especially in relation to infant and young child feeding practices and the importance of good nutrition during

pregnancy. Assurance of adequate iron intake and proper nutrition during adolescence is a pre-requisite for a society's prosperity; thus, state-funded supplementation should also be considered for those at need during these important developmental years. Perhaps most urgently, comprehensive nation-wide surveillance on the prevalence and country-specific etiology of anemia, including collection of data on iron status, must be conducted in order to direct future programs to prevent and control anemia. A multidisciplinary approach is essential to achieve these goals and the continued cooperation of the Cambodian government at the federal-, provincial- and community-level, together with international donors and development agencies will be the key to success.

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Review

Anemia in Cambodia: prevalence, etiology and research needs

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柬埔寨國人貧血之盛行率、病因及未來研究需求

由於貧血嚴重影響人類健康及帶來許多社經問題，使得貧血成為全球共同關注的公共衛生議題。本研究目的為探討柬埔寨國人貧血之現況，包括討論在柬埔寨貧血的具體病因與未來相關研究之需求。本篇研究使用標準化流程，蒐集了所有與柬埔寨貧血病因及盛行率相關之文獻。結果發現，學齡前兒童與育齡婦女的貧血盛行率資料較多，但缺乏學齡兒童、男性與老人族群的資訊。儘管過去十年來，有全國性營養相關計劃的推動，貧血依然是柬埔寨一個重要的公共衛生問題，尤其在女性與孩童族群。由於貧血為一種多面向的疾病，其病因包括營養及非營養因素，其中最主要導因為鐵質缺乏。本篇研究結論突顯全國性營養調查的急迫性，包括調查所有族群鐵質的相關指標及貧血盛行率等。惟有充分掌握本國貧血的概況及病因，才能發展有效的介入計畫以減少此疾病。

關鍵字：貧血、柬埔寨、病因學、盛行率、血紅素