ASSESSMENT OF VITAMIN B12 STATUS AFTER ILEAL RESECTION IN PAEDIATRIC PATIENTS MANAGED FOR INTUSSUSCEPTION AT KENYATTA NATIONAL HOSPITAL.

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STUDENT'S DECLARATION

I hereby declare that this dissertation proposal is my original work and has not been presented for a degree in any other university

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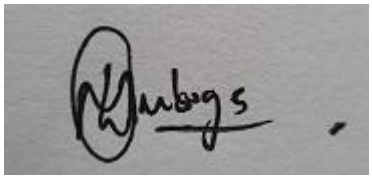
Signed:  Date: 10/ 09/ 2021

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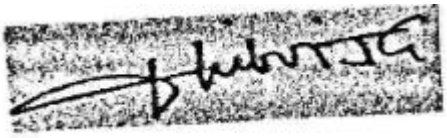

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LIST OF ABBREVIATIONS

KNH	KENYATTA NATIONAL HOSPITAL
PSOPC	PAEDIATRIC SURGICAL OUTPATIENT CLINIC
UON	UNIVERSITY OF NAIROBI
SPSS	STATISTICAL PACKAGE FOR SOCIAL SCIENCES
FL	FEMTOLITERS
G/DL	GRAMS PER DECILITER

OPERATIONAL DEFINITIONS

Paediatric age group	age less than 13 years.

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ABSTRACT

BACKGROUND

Vitamin B12 is absorbed at the terminal ileum. Deficiencies have been noted in patients following ileal resection such as in intussusception. Assessment of vitamin B12 levels and monitoring for deficiency in such patients could be a mandatory aspect of postoperative treatment.

STUDY OBJECTIVE

To assess the status of vitamin B12 after ileal resection in paediatric patients managed for intussusception at Kenyatta National Hospital.

METHODOLOGY

STUDY SETTING

Paediatric surgical outpatient clinic at Kenyatta National Hospital.

STUDY POPULATION

Paediatric patients who underwent ileal resection for intussusception at Kenyatta National Hospital between January 2009 and December 2019.

STUDY DESIGN

Descriptive cross-sectional study.

SAMPLE SIZE

The calculated sample size was 168 patients.

DATA MANAGEMENT

Blood was drawn from participants for vitamin B12 studies. The results, together with biodata and clinical information was entered into a data collection tool and analyzed. Continuous data was analyzed and summarized as means and standard deviations while categorical data was analyzed and displayed in charts by use of frequencies and proportions. Chi-square test, fisher's exact test and ANOVA were used to ascertain association among categorical and clinical variables. A P value of less than 0.05 will be considered statistically significant for 95% confidence interval.

ETHICAL CONSIDERATION

The parents or legal guardians of the children were taken through the process of informed consent. Confidentiality, anonymity, and privacy was observed throughout the study period. Institutional consent was requested from the Department of Surgery, University of Nairobi (UON), Ethics and Research Committee of KNH.

INTRODUCTION

Vitamin B12 is derived from animal-based diets such as meat, eggs and milk. The gastric parietal cells produce intrinsic factor which is necessary for vitaminB12 absorption in the terminal ileum. It is then used as a cofactor in synthesis of DNA, myelin and fatty acids. Deficiency therefore leads to neurocognitive and haematologic symptoms. It is stored in the liver and in cases of prolonged malabsorption, stores are depleted and deficiency occurs. (1)

Intussusception is invagination of a segment of intestine into the lumen of a distal segment, causing acute abdominal pain, intestinal ischaemia and obstruction. It typically presents between 6 and 36 months of age and is the most frequent cause of intestinal obstruction in children under 5 years. (2) Delayed presentation and diagnosis can lead to gangrene of the trapped intestinal segment (intussusceptum), often requiring segmental bowel resection. Ileocolic intussusception, which involves the terminal ileum accounts for 76% of all cases.(3)

In KNH, most patients with intussusception present late and therefore majority usually require bowel resection during surgery. It is however unknown whether these children, put at risk for vitamin b12 malabsorption, go on to develop deficiency as result. Previous studies done have demonstrated an association between intestinal resection in paediatric population with vitamin B12 deficiency. (4) (5). Some studies have also demonstrated normalization of vitamin B12 levels after an initial period of malabsorption following intestinal resection, advancing likelihood of adaptation in children. (6) . From these studies therefore, it is evident that there is risk of vitamin B12 deficiency following bowel resection, but there is no consensus as to how long after surgery deficiency occurs (latent period) and therefore there exists no common protocol for vitaminB12 supplementation following ileal resection.

Vitamin B12 deficiency leads to detrimental neurologic and psychiatric illness in children during a critical period of brain development. It also leads to anaemia, which has a stagnating effect on growth and nutritional status in children. This study therefore aimed to evaluate levels of vitamin B12 after intestinal resection and identify occurrence of deficiency. Results and data that

emanate will therefore help in formulation of local protocols for vitamin B12 level monitoring and supplementation after intestinal resection in children.

LITERATURE REVIEW

VITAMIN B12 PHYSIOLOGY

Booth and Mollin studied intestinal radiation signals after oral ingestion of radiolabeled vitamin B12. Increased concentrations were found in the ileum, providing evidence of the site of vitamin B12 absorption in bowel (7)

Vitamin B12 metabolism begins in the oral cavity and stomach with binding to R-proteins, for protection from gastric acidity. In the duodenum, pancreatic proteases degrade the R-protein freeing vitamin B12 for binding by intrinsic factor. In the terminal ileum, the vitamin B12-intrinsic factor complex attaches to specific receptors that mediate transport into the enterocyte and into portal blood. Intrinsic factor is released and vitamin B12 is now bound to transcobalamin 2 protein for transportation to the liver, where it is stored (8) . Concentration begins in the foetal stage and stores are usually adequate to sustain the infant for several months postpartum. Total body stores of vitamin B12 range between 2 to 5 mg.

Infants of vitamin B12 deficient mothers and infants eating low amounts of animal-based diet are susceptible to vitamin B12 deficiency between six to twelve months age(9). Grange DK and Finlay JL reported vitamin B12 deficiency in a breastfed infant following maternal subclinical vitamin B12 deficiency secondary to gastric bypass (10). Similar findings had already been noted by previous studies on infant vitamin B12 (11) (12)

In this study, infants of mothers with risk factors for vitamin B12 deficiencies, including vegetarian diet, history of gastric bypass or intestinal resection, and pernicious anaemia were excluded.

BOWEL RESECTION AND VITAMIN B12 DEFICIENCY

Different investigators have previously studied association of bowel resection and vitamin B12 deficiency in adult populations finding various results. There is a paucity of published paediatric data on vitamin B12 absorption after resection of the ileum in childhood (4)

Valman and Roberts published their findings on vitamin B12 absorption after resection of ileum in childhood. They found vitamin B12 malabsorption in 7 among 10 infants and children who had resection. They however found that despite abnormal absorption, deficiency did not occur for several years, with puberty being a high risk period (13). This study suggests that despite the impaired absorption resulting from ileal resection, the latent period to onset of vitamin B12 deficiency may be longer than is described in most text and literature, and therefore emphasizes need for a longer follow up period. Of note they determined the residual intestinal length to be a better indicator of absorption capacity rather than the length of resected intestine. Preservation of less than 15cm of terminal ileum was associated with vitamin B12 malabsorption.

M. Ahmed and H.R Jenkins retrospectively examined 18 children who had undergone resection of ileum due to Crohn's disease over a 10-year period. Eight of these children had between 30 to 50 cm of distal (terminal) ileum resected and the other 9 had less than 30 cm resected. No child was found to have vitamin B12 deficiency after surgery, for a period of between 1 to 8 years of follow up (4)

Findings from this study concur with Valman and Roberts findings that the latent period to development of vitamin B12 deficiency following bowel resection in children may be longer than previously thought. Neither of these studies answers the question on vitamin B12 supplementation in paediatric patients following ileal resection.

Dallman and Diamond in 1960 published a case report of a 36 hour old neonate who underwent extensive bowel resection from the proximal ileum to the ascending colon and developed symptomatic vitamin B12 deficiency 3 to 4 years after resection (14)

Clark and Booth, also reported a case of a 20 day old neonate who underwent extensive distal ileal resection and developed vitamin B12 deficiency at 13 months of age, about a year after resection (15)

These two case reports suggest that resection at a younger age of infancy may be associated with earlier onset of vitamin B12 deficiency possibly due to lesser hepatic stores.

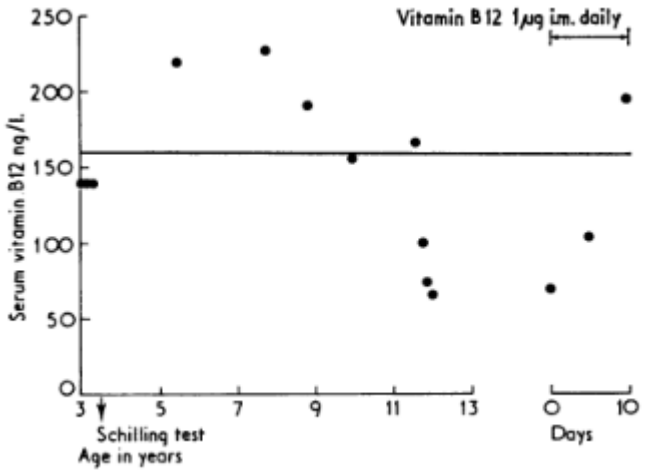
B.W Davies investigated the long-term consequences of limited ileal resection (less than 50cm) in infancy. They examined 24 children who had undergone a limited ileal resection for either necrotizing enterocolitis or intussusception. Vitamin B12 deficiency was isolated in one child who had undergone resection of 44cm of ileum and anastomosis 5 to 10 cm proximal to the ileocecal valve done (5). This finding suggests that even in limited ileal resections, which are performed mostly in our set up for intussusception, there still exists a risk of long-term vitamin B12 malabsorption and deficiency, and therefore need for supplementation. This finding also confirms Vallman and Roberts' observations that preservation of less than 15 cm of terminal ileum is associated with impaired absorption and deficiency of vitaminB12 and that the length of bowel resected has no significance compared to the site resected.

Evidence suggests paediatric intestines have the greatest potential for adaptation in response to loss of bowel length such as in short bowel syndrome. Vitamin B12 malabsorption after ileal resection has however been stated to be permanent in most literature. In 1992 however, B.C Ooi et al presented his case series of three children with documented vitamin B12 malabsorption secondary to ileal resection which became normal 6-8 years after the resection and they attributed this to a probable adaptation of the remaining small bowel to vitamin B12 absorption although spontaneous resolution of bacterial overgrowth was a possible explanation (6)

Despite evidence showing various degrees of association between ileal resection and vitamin b12 deficiency, papers and guidelines on follow up care after surgery in children do not include screening for B12 deficiency. In children, the commonest indication of ileal-colic resection is in treatment of inflammatory bowel disease and practice guidelines on surgical strategies in its management in children do not include vitamin b12 deficiency screening. This gap informs part of justification for this study as information may lead to development of institutional practice guidelines on standard of care after ileal resection in children. (16)

LATENT PERIOD BETWEEN BOWEL RESECTION AND VITAMIN B12 DEFICIENCY

In Valman and Roberts' study of 12 paediatric patients' vitamin B12 levels after resection of ileum, a single patient was followed up from age 3 to 11 years with the aim of describing how long after surgery deficiency begins to manifest.



(13)

The findings were progressively normal vitamin B12 levels until the age 10 years associated with onset of puberty when levels fell precipitously. They postulated the pubertal growth spurt as a possible factor associated with deficiency. Booth observed that low serum vitamin B12 levels occur at a shorter interval after resection than in adults, therefore discussing age at resection as a possible factor determining onset of deficiency.

MEASUREMENT OF VITAMIN B12 LEVEL

Serum vitamin B12 levels are measured using a competitive chemiluminescence assay that has a sensitivity of approximately 95% and a specificity of approximately 80%. Serum levels are classified as follows: Above 221 picomole per liter - normal

148 to 221 picomole per liter – borderline

Below 148 picomole per liter – low, consistent with deficiency (17)

The WHO guideline on vitamin B12 deficiency classifies deficiency as plasma levels less than 150 picomole per liter (18)

CLINICAL MANIFESTATIONS OF VITAMIN B12 DEFICIENCY

In children, neurologic findings can vary widely and include; weakness, abnormality in proprioception, paraesthesia, obtundation, coma, ataxia, coma, tremors, chorea, personality change, memory loss, developmental delay, hypotonia and seizures. Chronicity of deficiency in developing children is directly related to severity of neurologic impairments and failure of complete response to treatment (19)

Haematological manifestations range from macrocytic anaemia to overt pancytopenia (19)

In majority of the cases, symptoms are reversible with initiation of supplementation, but irreversible differences have been described in literature.

Rahul Jain et al reported a case series of 14 paediatric patients with vitamin B12 deficiency presenting with neurodevelopmental delay (20).1 patient presented with seizures, a complication described in literature.

Demir N et al evaluated 41 infants who had been admitted and diagnosed with vitamin B12 deficiency. They analyzed mental, neuromotor and social developments. They found weakness, tremors, hypotonia, motor retardation and convulsions in all the patients as features of neurological disease. In all these patients , treatment with vitamin B12 provided full recovery.(21)

AGE AND VITAMIN B12 DEFICIENCY

Age independently is not a risk factor for vitamin B12 deficiency in children. In normal pediatric patients without any known risk factor for vitaminB12 deficiency, there is no age that has been associated with a deficiency of vitamin B12. However, in vitamin B12 deficient mothers, decreased foetal vitamin storage coupled with low postnatal intake in breastmilk causes a likely occurrence of infantile vitamin B12 deficiency usually between three to four months of age. (22)

STUDY JUSTIFICATION

Intussusception is the commonest cause of infantile intestinal obstruction in K.N.H with an average of 40 cases per year. Because of late presentation, the majority end up undergoing bowel resection involving the distal ileum, the main site of vitamin B12 absorption. Literature from other populations shows evidence of an association between bowel resection and occurrence of vitamin B12 deficiency in children. Children undergoing bowel resection for intussusception in K.N.H are at risk of vitamin B12 deficiency but the prevalence is not known.

Clinical sequalae of vitamin B12 deficiency in paediatrics leads to permanent neurological and cognitive impairment and therefore establishing the prevalence in our population will help in formulation of protocols for adequate monitoring and supplementation.

RESEARCH QUESTION

What is the status of vitamin B12 levels after ileal resection in paediatric patients managed for intussusception in Kenyatta National Hospital?

STUDY OBJECTIVES

Broad Objective

To assess the status of vitamin B12 after ileal resection in Paediatric patients managed for intussusception at Kenyatta National Hospital.

Specific Objectives

1. To measure the levels of vitamin B12 after ileal resection in paediatric patients managed for intussusception at Kenyatta National Hospital.
2. To determine association between the duration post ileal resection and vitamin B12 levels in paediatric patients managed for intussusception at Kenyatta National Hospital.
3. To determine the prevalence of vitamin B12 deficiency after ileal resection in paediatric patients managed for intussusception at Kenyatta National Hospital.

MATERIALS AND METHODS

Study design

This was a cross-sectional study.

Study area

The study was conducted at KNH. This is a national teaching and referral hospital, with 2000 bed capacity. It serves as the teaching hospital for the University of Nairobi, College of Health Sciences for both the undergraduate and postgraduate programs. This study took place in the paediatric surgical outpatient clinic, housed at clinic number 23, which is where patients are usually followed up post operatively.

Study Population

Paediatric patients who underwent bowel resection for intussusception at KNH between January 2009 and December 2019.

Inclusion criteria

All paediatric patients who had bowel resection for intussusception at KNH between the year 2009 and 2019 and consented to the study.

Exclusion criteria

Any patients on vitamin B12 supplementation from other causes.

Patients with comorbidities affecting vitamin B12 metabolism including autoimmune pernicious anaemia, Crohn's disease, celiac disease and severe protein energy malnutrition.

Patients known to be on vegetarian diet.

Patients whose mothers carry risk of vitamin B12 deficiency during breastfeeding period. These included mothers on vegetarian diet, mothers with history of gastric by-pass or ileal resection surgery and pernicious anaemia.

Sample size

Data from KNH health information records department shows there is an average of about 40 cases of intussusception in children in KNH per year, with a resection rate of about 75%. The study population was therefore 300 children who had undergone surgery for intussusception with bowel resection between January 2009 and December 2019.

Using Daniel formula with finite population correction the sample size (23)

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1)+Z^2P(1-P)}$$

Where n'= desired sample size

N= population size (300)

P= expected proportion (50%)

D= precision (5%)

Z= 1.96

n was therefore equal to 168

Sampling technique

Consecutive non-random recruitment of patients who met the inclusion criteria until the desired sample size was reached.

Consenting procedure

The study was explained to the eligible patient in the company of a parent or guardian by the researcher or the research assistant. Informed and written consent was sought from the parent or guardian. An assent form was completed by the patient if he was 6-17 years old. The patient in the company of the parent or guardian was taken through the process of blood collection as per the patient's age.

Blood sample collection and vitamin B12 assay procedure

The participant in the company of the parent or guardian was taken to the paediatric laboratory where a certified phlebotomist met them to draw a blood sample. Skin was swabbed with spirit, and a 25-gauge needle and 5ml syringe were used to draw 2mls of blood via venipuncture, and a dry cotton swab was placed gently after venipuncture. This blood was immediately emptied into a red vaccutainer containing a clot activator. Sample was then processed using the Cobas ®6000 machine to form serum for testing vitamin B12 levels. Serum was then mixed with the Elecsys vitamin B12 II reagent in the cobas® e 601 module as per manufacturers specifications to give vitamin B12 test results in picograms per milliliter.

This result was then converted into picomoles/litre (W.H.O's S.I unit) using an online scientific converter and therefore results were entered and analyzed as picomoles per litre. (24)

Further, clinical evaluation for features of vitamin B12 deficiency and a full blood count were done for clinical correlation as part of quality assurance. (25) The specific parameters evaluated are highlighted on the data collection form. (26) Blood sample collection for full blood count assessment was as for vitaminB12 assay described above. However, it was emptied into an EDTA (ethylenediaminetetraacetic acid) containing purple top vacutainer for haematological tests and processed for full blood count test using the sysmex XN-1000 analyzer machine.

These analyses were done after each clinic and there was no batch analysis and therefore no sample storage.

DATA MANAGEMENT

Collected data was sorted, cleaned, categorized, and entered into the statistical software package SPSS version 24 (Chicago) for analysis. The folder containing the data was password-protected and uploaded to a cloud storage drive and back up was done daily to prevent missing entries. Continuous data was analyzed and summarized as means and standard deviations while categorical data was analyzed and displayed in charts by use of frequencies and proportions. Chi-square test and fishers exact test was used for bivariate analysis, to establish the correlations between presence of vitamin B12 deficiency and clinic-demographic characteristics of the study population. Analysis of variance (ANOVA) and Independent sample T tests were used to establish association between quantitative and other clinicodemographic parameters. A P value of less than 0.05 was the cutoff for statistical significance. Data is presented as figures, texts, and tables.

ETHICAL CONSIDERATION

Informed Consent and Assent: The parents or legal guardian in the presence of the children in this study were informed by the researcher on the purpose and rationale of the study. Participation was voluntary and the participants were allowed to leave the study at any specified time according to their discretion. A consent form was signed by both the parent or legal guardian and the researcher. An assent form was signed by children aged 6-17 years once the patient agreed to participate in the study.

Confidentiality: All participants remained anonymous and identification was done by a unique patient identification number. Confidentiality and privacy were observed throughout the duration of the study.

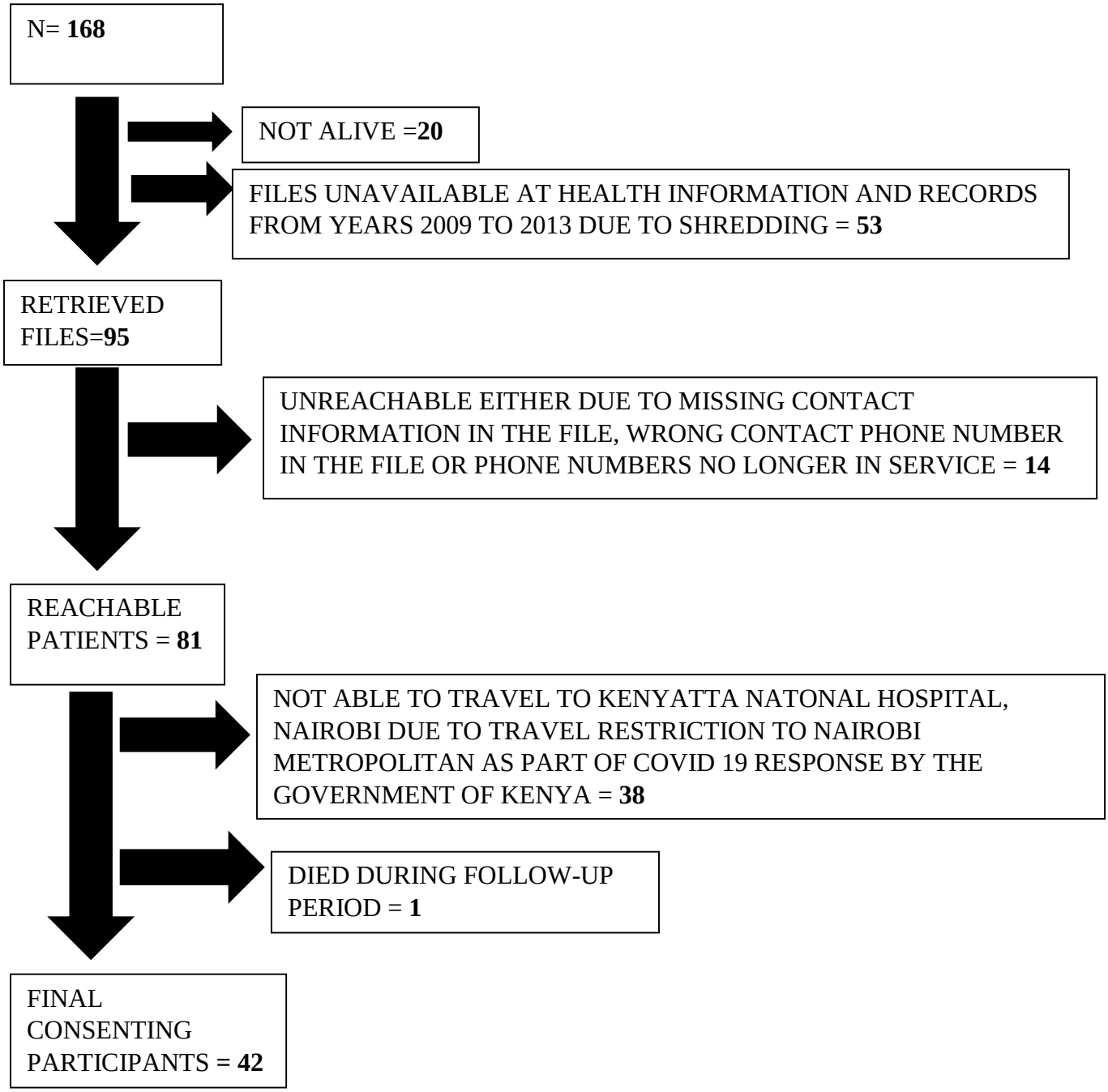
Research Approval: Institutional consent was sought from the University of Nairobi, department of surgery and the Ethics and Research committee of KNH.

Quality Assurance

This was ensured by adhering to the standard aseptic procedure during venipuncture. KNH medical laboratory is certified by International Organization for Standardization (ISO 15189: 2012) ensuring quality and competence in the laboratory and the specific lab tests performed here in are in the scope of the accreditation. Collected samples were analyzed using the criteria established by Clinical and Laboratory Standards Institute (CLSI). Quality control materials were used to verify quality of testing.

RESULTS

SAMPLE SIZE



DESCRIPTIVE STATISTICS AND DEMOGRAPHICS

A total of 42 participants were recruited into the study. Only one (2.4%) participant was female. The rest were males. The mean age was 5.0±2.2 years and ranged from 1yr to 11yrs 9months. The median age at surgery was 8months, interquartile range 6-16.5months. Median duration post-surgery was 53months, interquartile range 30.5-67.3months. All participants were resident in Nairobi. The demographic characteristics of the study population is summarized in the table below;

Characteristics		**Frequency (%)**
Age(years)	0-2	4(9.5)
	3-4	6(14.3)
	5-6	17(40.5)
	7-8	7(16.7)
	>9	8(19.0)
Age at surgery (Months)	<12	31(73.8)
	13-24	8(19.0)
	25-36	1(2.4)
	37-48	0
	49-60	2(4.8)
Duration post-surgery (Months)	<12	3(7.1)
	13-24	5(11.9)
	25-36	5(11.9)
	37-48	7(16.7)
	49-60	9(21.4)
	>61	13(31.0)
Gender	Male	41(97.6)
	Female	1(2.4)

Table 1: Demographic characteristics

VITAMIN B12 LEVELS

Characteristics		**Frequency (%)**
Vitamin B12	Normal	31(73.8)
	Borderline	5(11.9)
	Low	6(14.3)
B12 deficiency	Yes	11(26.2)
	No	31(73.8)

Table 2: vitamin B12 levels

In this study, a majority of the participants, at 73.8% were found to have normal vitamin B12 levels after ileal resection.

Six participants, representing 14.3 % however were found to have levels consistent with vitamin B12 deficiency.

DURATION POST ILEAL RESECTION AND VITAMIN B12 LEVELS

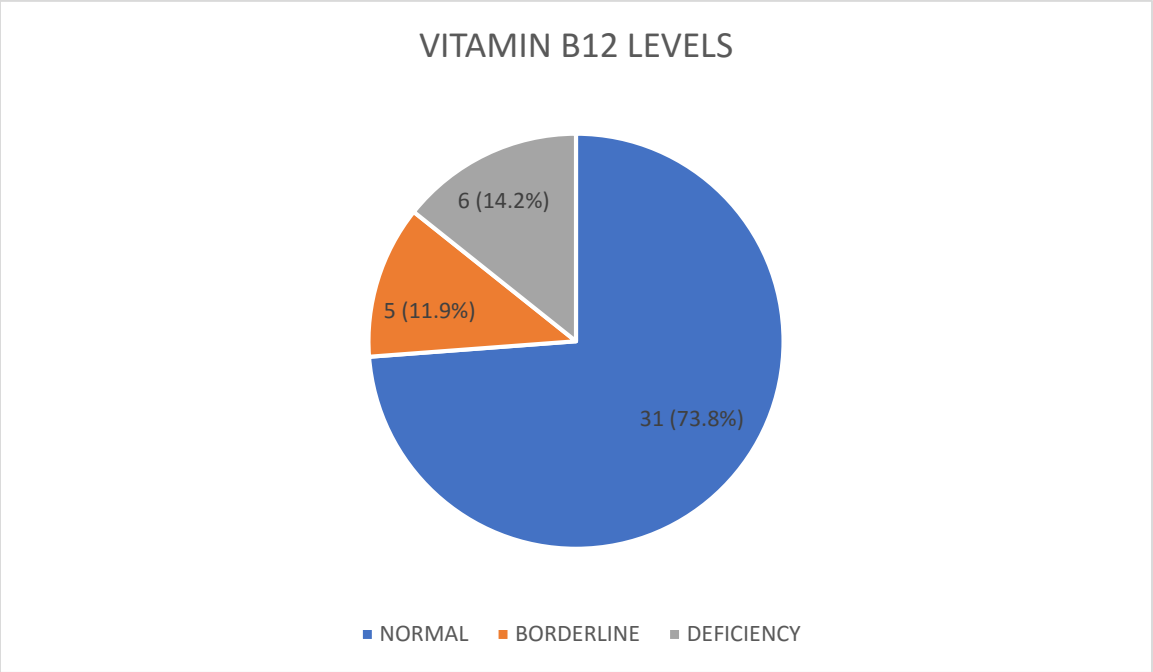
Characteristic		**Vitamin B12 deficiency**		**Total**	**Sig.**
		Yes	**No**		
Age `	0-2	0	4(100)	4	**0.03**
	3-4	0	6(100)	6	
	5-6	5(29.4)	12(70.6)	17	
	7-8	5(79.4)	2(28.6)	7	
	>9	1(12.5)	7(87.5)	8	
Mean age	ANOVA	6.3±1.4	4.5±2.3		**0.02**
Duration post-surgery	<12	0	3(100)	3	0.24
	13-24	0	5(100)	5	
	25-36	0	5(100)	5	
	37-48	2(71.4)	5(28.6)	7	
	49-60	3(66.7)	6(33.3)	9	
	>61	6(53.8)	7(46.2)	13	
Median duration post-surgery	ANOVA	61	42		**0.008**

Table 3: duration post ileal resection and vitamin b12 levels

On bivariate analysis, children with vitamin B12 deficiency were found to have a longer duration post-surgery (latency) than those without deficiency, with medians of 5 years and 3.5 years respectively, P value of 0.008.

Notably also, the mean age was significantly higher among children with vitamin B12 deficiency than those without deficiency.

PREVALENCE OF VITAMIN B12 DEFICIENCY AFTER ILEAL RESECTION



Prevalence of vitamin B12 deficiency was found to be 26.2 %, and included patients with both borderline and overt deficiency.

CLINICAL MANIFESTATIONS OF VITAMIN B12 DEFICIENCY

None of the participants were symptomatic and there were no signs of megaloblastic anemia present.

The following is a table showing the laboratory measurements;

Characteristics		**Frequency (%)**
Haemoglobin	Normal	30(71.4)
	Anaemia	12(21.6)
Type of anaemia based on MCV values	Normal	23(54.8)
	Microcytic	14(33.3)
	Megaloblastic	5(11.9)
Platelet	Normal	33(78.6)
	Thrombocytopenia	1(2,4)
	Thrombocytosis	8(19.0)

TABLE 4: laboratory measurements

The following is a table showing bivariate analysis of laboratory measurements;

Characteristic		**Vitamin B12 deficiency**		**Total**	**Sig.**
		Yes	**No**		
Haemoglobin	Normal	5(16.7)	25(83.3)	30	**0.049**
	Anaemia	6(50.0)	6(50)	12	
Type of anaemia based on MCV values	Normal	5(21.7)	18(78.3)	23	**<0.001**
	Microcytic	1(7.1)	13(92.9)	14	
	Megaloblastic	5(100)	0	5	
Platelet	Normal	8(24.2)	25(75.8)	33	0.75
	Thrombocytopenia	0	1(100)	1	
	Thrombocytosis	3(37.5)	5(62.5)	8	

Table 5: bivariate analysis of laboratory measurements

DISCUSSION

Vitamin B12 is derived from animal based diets and is absorbed in the terminal ileum. The commonest anatomical type of intussusception involves the terminal ileum and late presentation with gangrene often leads to resection of segment containing the terminal ileum. These children could therefore be at risk for vitamin B12 deficiency following surgery. Literature from previous studies has shown an association between intestinal resection in the paediatric population and vitamin B12 deficiency. Other investigators have demonstrated normalization of vitamin B12 levels after an initial period of malabsorption and deficiency following intestinal resection, advancing likelihood of adaptation to vitamin B12 absorption in children. Sequelae of vitamin B12 deficiency leads to detrimental neuropsychiatric and haematological disorders in children, which are reversible if screening, diagnosis and intervention by vitamin B12 supplementation is initiated early. In K.N.H, majority of infants and children with intussusception present late, and this has led to resection rates of more than 50% each year. This therefore puts the majority of these children at risk for vitamin B12 deficiency, therefore justifying undertaking of this study that aimed at measuring vitamin B12 levels, determining its association with duration post ileal resection and the prevalence of its deficiency among paediatric patients managed for intussusception at K.N.H. A cross-sectional study was thus conducted at the paediatric surgical outpatient clinic of K.N.H, beginning in the month of July, 2020, with an initial calculated sample size of 168 paediatric patients. Consenting participants were seen at the PSOPC where evaluation was done as per the data collection tool specifications. They then proceeded to the designated KNH laboratory for lab procedures, the results of which were used to complete the data collection tool filling. Participants were then released from the PSOPC and the collected data stored safely. On completion of collection, data was analyzed and presented as figures, tables and text.

Demographic results of this study show that all the participants' residence was the Nairobi metropolitan area, in spite of K.N.H being a national referral hospital. Like many sectors in 2020, this study was adversely affected by the ongoing COVID-19 pandemic.(27) From the month of March 2020, K.N.H initiated response measures to the pandemic that included closure

of all outpatient clinics, which in later months was loosened by allowing opening of clinics for urgent cases. In the following month of April, on 6th, the Government of Kenya issued travel restriction on entry into Nairobi metropolitan area. (28) This resulted in majority of anticipated participants from outside Nairobi declining consent citing major travel hindrances. Coupled with suboptimal running of the outpatient clinics during the period of data collection, these two factors resulted in an adverse reduction of the study participants to 42 from the calculated sample size, resulting in significant reduction of power of the study for generalization to similar populations. Nevertheless, the results yielded significant findings that can act as a landmark and reference point for a future prospective study with a larger sample size.

Patient characteristics and demographic results show that of the 42 children, 41 (97.6%) were males and 1(2.4%) female giving a ratio of 41:1. Worldwide, studies from different populations show an overall male predominance, similar to this study. World Health Organization reference on intussusception shows the highest male to female ratios from African and Asian populations at 8:1 and 9:1 respectively. (29) In Tanzania, a study done by Phillipo et al, with a total of 56 children managed for intussusception found a male to female ratio of 3.3:1. (30) Similarly, in a study on infants with intussusception from 7 sub-Saharan African countries including Kenya, a male preponderance was seen at 59%. (31) A study done on Kenyan infants with intussusception at the Moi Teaching and referral Hospital recruited 36 children and found a male to female ratio of 3.5: 1. (32) Therefore, similar to other studies from Kenyan, African and other populations, a male predominance of intussusception was identified in this study. However, unlike these studies, findings of this study have shown a very high male to female ratio. The reason for this finding is unclear and such difference has not been described previously in literature.

In R.T Kuremu's study of 36 Kenyan paediatric patients with intussusception done at the Moi Teaching and Referral hospital in Eldoret, the median age at disease diagnosis and management was found to be 8 months, similar to results from this study that show median age at diagnosis and management of 8 months. These findings are also in line with results from studies from other African populations, which give a median age of intussusception at 29 weeks (approximately 7.25 months). (2)

On measurement of vitamin B12 levels in this study, majority of the participants (73.8 %) were found to have normal levels, 11.9 % had levels consistent with borderline deficiency and 14.3 % had levels consistent with overt deficiency. Comparing the levels with duration post ileal resection, those with deficiency were found to have significantly longer duration than those without deficiency with medians of 5 years and 3.5 years post ileal resection respectively. B.W Davies et al examined 24 children who had undergone ileal resection for intussusception and necrotizing enterocolitis and in their study, they found vitamin B12 deficiency in 1 patient. (5) Their findings are in keeping with this study where vitamin B12 deficiency was also identified on measurement of vitamin B12 levels after ileal resection in paediatrics, even though his population did not only include intussusception but also necrotizing enterocolitis. Both studies demonstrate that vitamin B12 deficiency is a potential long-term hazard after ileal resection in children, including resection for treatment of intussusception. Valman and Roberts studied 10 infants who had undergone resection of ileum in childhood and found that in spite of vitamin B12 malabsorption being demonstrated in 7 of the 10, deficiency had occurred in only 1 patient who had a precipitous fall in vitamin B12 levels at the age of 10 years. They attributed this to the accelerated pubertal growth spurt. At the time of publishing, 3 of the children in their series still had normal vitamin B12 levels at more than 5 years post ileal resection. This long latency period has been attributed to presence of large hepatic stores of vitamin B12 in adults by Booth et al, but it remains uncertain in the paediatric population. However, in two reports of ileal resection in the neonatal period by Clark and Booth (15), and Dallman and Diamond (14), deficiency was reached within 4 years, demonstrating that latency could be shorter, more so in resection done in the neonatal age group.

This study is the first of a Kenyan and African paediatric population assessing the status of vitamin B12 after ileal resection for intussusception, and it has demonstrated that there is a potential risk of vitamin B12 deficiency in this population, similar to reports from other populations, with a median latency period of 5 years to onset of deficiency.

In this study, out of the 42 children enrolled, 6 patients (14.2%) were established to have overt vitamin B12 deficiency, while 5 children had borderline deficiency, hence giving an overall prevalence of vitamin B12 deficiency at 26.2 %. This is the first study attempting to establish vitamin B12 deficiency prevalence among this at risk population in literature. B.W Davies found

vitamin B12 deficiency in 1 of 24 children following ileal resection (4.2%) (5), while Valman and Roberts established deficiency in 1 of 10 infants who had undergone ileal resection in childhood, (10%) (13). However unlike these previous reports, Ahmed and Jenkins in their study examining 18 children who had undergone distal terminal ileal resection of up to 50 cm for Crohns disease found no child with vitamin B12 deficiency for a period of up to 8 years of follow up. (4) Evidently compared to these previous reports, this study gives a higher prevalence of vitamin B12 deficiency in our population. This could be as a result of an overall higher prevalence of under nutrition among population of Kenyan children leading to reduced hepatic stores of vitamin B12 compared to other populations. A study by Bwibo et al showed prevalence of low vitamin B12 levels (less than 148 pmol/l) to be very high in Kenyan school children. (33, 34) In this study, baseline vitamin B12 levels were not captured at the time of diagnosis for intussusception.

STUDY LIMITATIONS

The significant reduction of the enrolled participants from the original study sample size occasioned by the COVID-19 pandemic lead to a reduction in power of the study and therefore in spite of the study showing association between vitamin B12 levels and duration post ileal resection, the results cannot be generalized to our population without a further follow up study to affirm the results.

In this study, baseline vitamin B12 levels at the time of diagnosis of intussusception were not available. It is important to have a baseline level so as to differentiate between a new onset vitamin B12 malabsorption after ileal resection from a preexisting vitamin B12 deficiency prior to diagnosis of intussusception, especially after two studies by Bwibo et al showed a high prevalence of vitamin B12 deficiency among school going children in Kenya. (33, 34)

This study did not include data on length of resected and residual bowel and specific site of ileal resection. Valman and Roberts determined residual intestinal length to be a good indicator of absorption capacity rather than length of resected intestine, and that preservation of less than 15cm of terminal ileum was associated with vitamin B12 malabsorption. (13) In view of already documented high community prevalence of vitamin B12 deficiency in our population (33,34), such information would have enhanced a stronger association of vitamin B12 deficiency with ileal resection for intussusception.

RECOMMENDATIONS

A follow up study after the COVID-19 pandemic restrictions is recommended to better capture different demographic characteristics and a larger sample size especially since prevalence of vitamin B12 deficiency has been established at 26.2% in this study.

Determination of baseline vitamin B12 levels for patients undergoing ileal resection for intussusception and subsequent monitoring of levels for up to 5 to 6 years of age. This is however a weak recommendation owing to the sample size limitation and requires undertaking a larger follow up study to confirm latency period to onset of vitamin B12 deficiency after ileal resection for intussusception in our population.

A multicenter study is recommended as a follow up study to improve on the study power and generalization of findings to our population.

CONCLUSION

Vitamin B12 deficiency post ileal resection for intussusception was established in this study with a prevalence of 26.2%, and patients with deficiency were found to have a longer median duration post ileal resection compared to patients with normal vitamin B12 levels. Follow up studies with a larger sample size is recommended to further strengthen results of this study and provide the threshold needed to inform establishment of hospital based guidelines for monitoring vitamin B12 levels in paediatric patients post ileal resection for intussusception in our population.

REFERENCES

1. Ankar A, Kumar A. Vitamin B12 Deficiency (Cobalamin). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 [cited 2020 Jan 28]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK441923/

2. Clark AD, Hasso-Agopsowicz M, Kraus MW, Stockdale LK, Sanderson CFB, Parashar UD, et al. Update on the global epidemiology of intussusception: a systematic review of incidence rates, age distributions and case-fatality ratios among children aged <5 years, before the introduction of rotavirus vaccination. Int J Epidemiol. 2019 Aug 1;48(4):1316–26.

3. Hazra NK, Karki OB, Verma M, Rijal D, De A, Nath B. Intussusception in Children: A Short-Term Analysis in a Tertiary Care Hospital. Am J Public Health Res. 2015 Jul 1;3(4A):53–6.

4. Ahmed M, Jenkins HR. Vitamin B-12 in Crohn's disease patients with small bowel surgery. Arch Dis Child. 2004 Mar 1;89(3):293–293.

5. Davies BW, Abel G, Puntis JWL, Arthur RJ, Truscott JG, Oldroyd B, et al. Limited ileal resection in infancy: The long-term consequences. J Pediatr Surg. 1999 Apr 1;34(4):583–7.

6. Ooi BC, Barnes GL, Tauro GP. Normalization of Vitamin B12 absorption after ileal resection in children. J Paediatr Child Health. 1992;28(2):168–71.

7. Booth CC, Mollin DL. The site of absorption of vitamin B12 in man. Lancet. 1959;1:18–21.

8. Schjønsby H. Vitamin B12 absorption and malabsorption. Gut. 1989 Dec;30(12):1686–91.

9. Pepper MR, Black MM. B12 in fetal development. Semin Cell Dev Biol. 2011 Aug 1;22(6):619–23.

10. Grange DK, Finlay JL. Nutritional Vitamin B12 Deficiency in a Breastfed Infant Following Maternal Gastric Bypass. Pediatr Hematol Oncol. 1994 Jan 1;11(3):311–8.

11. Jathar VS, Kamath SA, Parikh MN, Rege DV, Satoskar RS. Maternal Milk and Serum Vitamin B12, Folic Acid, and Protein Levels in Indian Subjects. Arch Dis Child. 1970 Apr 1;45(240):236–41.

12. Honzik T, Adamovicova M, Smolka V, Magner M, Hruba E, Zeman J. Clinical presentation and metabolic consequences in 40 breastfed infants with nutritional vitamin B12 deficiency – What have we learned? Eur J Paediatr Neurol. 2010 Nov 1;14(6):488–95.

13. Valman HB, Roberts PD. Vitamin B12 absorption after resection of ileum in childhood. Arch Dis Child. 1974 Dec 1;49(12):932–5.

14. Dallman PR, Diamond LK. Vitamin B12 deficiency associated with disease of the small intestine: Observations on an infant following extensive small bowel resection. J Pediatr. 1960 Nov 1;57(5):689–94.

15. Clark ACL, Booth CC. Deficiency of Vitamin B12 After Extensive Resection of the Distal Small Intestine in an Infant. Arch Dis Child. 1960 Dec;35(184):595–9.

16. Baillie CT, Smith JA. Surgical strategies in paediatric inflammatory bowel disease. World J Gastroenterol WJG. 2015 May 28;21(20):6101–16.

17. Oberley MJ, Yang DT. Laboratory testing for cobalamin deficiency in megaloblastic anemia. Am J Hematol. 2013 Jun;88(6):522–6.

18. de Benoist B. Conclusions of a WHO Technical Consultation on Folate and Vitamin B $_{12}$ Deficiencies. Food Nutr Bull. 2008 Jun;29(2_suppl1):S238–44.

19. Dobrozsi S, Flood VH, Panepinto J, Scott JP, Brandow A. Vitamin B12 deficiency: The great masquerader: Vitamin B12 Deficiency in Children. Pediatr Blood Cancer. 2014 Apr;61(4):753–5.

20. Jain R, Singh A, Mittal M, Talukdar B. Vitamin B12 Deficiency in Children: A Treatable Cause of Neurodevelopmental Delay. J Child Neurol. 2015 Apr 1;30(5):641–3.

21. Demir N, Koc A, Üstyol L, Peker E, Abuhandan M. Clinical and neurological findings of severe vitamin B12 deficiency in infancy and importance of early diagnosis and treatment. J Paediatr Child Health. 2013 Oct;49(10):820–4.

22. Rasmussen SA, Fernhoff PM, Scanlon KS. Vitamin B12 deficiency in children and adolescents. J Pediatr. 2001 Jan;138(1):10–7.

23. Naing L, Winn T, Rusli BN. Practical Issues in Calculating the Sample Size for Prevalence Studies. :6.

24. Vitamin B12 (Cobalamin, Cyanocobalamin) conversion to pmol/L, pg/mL, pg/dL, pg/100mL, pg%, pg/L, ng/L . Online converter from conventional units to SI units | UNITSLAB.COM [Internet]. [cited 2020 Jun 3]. Available from: https://unitslab.com/node/141

25. Langan RC, Goodbred AJ. Vitamin B12 Deficiency: Recognition and Management. Am Fam Physician. 2017 Sep 15;96(6):384–9.

26. afp20170915p384-t2.gif (GIF Image, 814 × 1543 pixels) - Scaled (42%) [Internet]. [cited 2020 Jun 3]. Available from: https://www.aafp.org/afp/2017/0915/hi-res/afp20170915p384-t2.gif

27. Coronavirus disease (COVID-19) – World Health Organization [Internet]. [cited 2021 Apr 25]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019

28. Public Legal Information on Kenya's Response to COVID-19 | Kenya Law [Internet]. [cited 2021 Jan 25]. Available from: http://kenyalaw.org/kenyalawblog/kenyas-response-to-covid-19/

29. Organization WH. Acute intussusception in infants and children : incidence, clinical representation and management : a global perspective. 2002 [cited 2021 Apr 24]; Available from: https://apps.who.int/iris/handle/10665/67720

30. Chalya PL, Kayange NM, Chandika AB. Childhood intussusceptions at a tertiary care hospital in northwestern Tanzania: a diagnostic and therapeutic challenge in resource-limited setting. Ital J Pediatr. 2014 Mar 11;40(1):28.

31. Pindyck T, Parashar U, Mwenda JM, Tadesse A, Armah G, Omore R, et al. Risk Factors Associated With Increased Mortality From Intussusception in African Infants. J Pediatr Gastroenterol Nutr. 2020 Jan;70(1):20–4.

32. Kuremu RT. Childhood intussusception at the Moi teaching and Referral Hospital Eldoret: management challenges in a rural setting. East Afr Med J. 2004 Sep;81(9):443–6.

33. McLean ED, Allen LH, Neumann CG, Peerson JM, Siekmann JH, Murphy SP, et al. Low plasma vitamin B-12 in Kenyan school children is highly prevalent and improved by supplemental animal source foods. J Nutr. 2007 Mar;137(3):676–82.

34. Siekmann JH, Allen LH, Bwibo NO, Demment MW, Murphy SP, Neumann CG. Kenyan school children have multiple micronutrient deficiencies, but increased plasma vitamin B-12 is the only detectable micronutrient response to meat or milk supplementation. J Nutr. 2003 Nov;133(11 Suppl 2):3972S-3980S.

APPENDIX 1: STUDY TIMELINE

Activity	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Mar 2020	Apr 2020	May 2020	Jun 2020	Jul 2020	Aug 2020	Sep 2020	Oct 2020	Nov 2020	Dec 2020	Jan 2021
Proposal development																
Ethical Approval																
Data collection																
Data Analysis																
Dissertation Writing and presentation																

APPENDIX II: CONSENT FORM (ENGLISH VERSION)

ASSESSMENT OF VITAMIN B12 STATUS AFTER ILEAL RESECTION IN PAEDIATRIC PATIENTS MANAGED FOR INTUSUSSCEPTION AT KENYATTA NATIONAL HOSPITAL

This informed consent form is for parents or guardians with children who have undergone surgery for intussusception. We are requesting these patients to participate in this research project whose title is " **Assessment of vitamin B12 status after ileal resection in paediatric patients managed for intussusception at Kenyatta National Hospital**"

Principal Investigator: Dr. Leon Onkunya

Institution: Department of Surgery, School of Medicine- University of Nairobi

Supervisors: Dr. F. Osawa, Dr. P. Mwika, Dr. S. Shahbal, Dr. Timothy Jumbi

This informed consent has three parts:

1. Information sheet (to share information about the research with you)
2. Certificate of Consent (for signatures if you agree to take part)
3. Statement by the researcher

You will be given a copy of the full informed consent form.

Part 1: Information sheet

Introduction

My name is Dr. Leon Onkunya, a postgraduate student in Pediatric Surgery at the University of Nairobi. I am conducting a study entitled "Assessment of vitamin B12 status after ileal resection in paediatric patients managed for intussusception at Kenyatta National Hospital"

Purpose of the study

Some patients who have had surgical management of intussusception undergo excision of the terminal ileum. This is the site of vitamin B12 absorption. Hence these patients are at risk of vitamin B12 malabsorption with deleterious neurological and hematological consequences. The prevalence and timing of vitamin B12 deficiency in such patients is not known in our setup.

Study Participation

I am inviting the child under your care to participate in my study. You will be given an opportunity to ask questions before you decide. Participation in this study is voluntary. If you agree to participate, you will be asked to sign a consent form. No payments will be made due to your participation in the study.

Benefits of participation

Participation in the study will help to assess whether your child has deficient vitamin B12 after ileal resection. If found to be deficient, they will be put on supplementation to avoid the negative consequences of Vitamin B12 deficiency. The results of this study will also be used to assess which patients are most at risk and to develop protocols for follow-up of patients who have had ileal resection following intussusception.

Risk of Participation

Your child's involvement in this research will be through filling of a data collection form and the collection of a blood sample for analysis. Your child will not be exposed to any additional risk if you consent to participate.

Right to decline or withdraw

You are free to withdraw from the study at any time. The refusal to participate or withdraw from the study will not in any way compromise the quality of care and treatment given to the patient.

Confidentiality

Any information that is obtained from you in this research will be treated with utmost confidentiality. The patient's name shall not be used.

Sharing of results

Knowledge gained from this study will be shared with other experts through conferences and publications. Confidentiality will be maintained.

Cost and Compensation

There shall be no extra cost incurred by you from participation in the study and there is also no compensation.

Contacts of relevant parties

1. **Primary Investigator**

   Dr. Leon Onkunya

   Resident, Department of Surgery, University of Nairobi

   P.O Box 19676 KNH, Nairobi 00202

   Mobile Phone 0720955652

2. **Research Assistant**

   Dr. Robert M. Mugo

   Resident, Department of Surgery, University of Nairobi

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Dr. Timothy Jumbi

Consultant Pediatric Surgery

Kenyatta National Hospital

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Tel: 0202726300

Part 2: Consent form

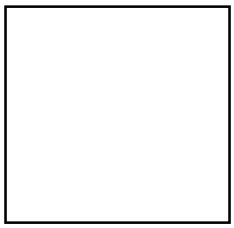
Statement of consent by parent or guardian

I……freely give consent for my child

Name……to take part in the study "Assessment of vitamin B12 status after ileal resection in paediatric patients managed for intussusception at Kenyatta National Hospital."

I have been informed and have understood that my child's participation is entirely voluntary. I understand the information given about the study and I have had the opportunity to ask questions and all my concerns have been addressed.

I have the freedom to decline to participate in the study at any time



Signature or left thumb print (Parent/Guardian) ……. Date…….

Statement by witness if parent or guardian is illiterate

I have witnessed the accurate reading of the consent form to the participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness …….

Signature of witness…….

Date……

PART III: Statement by the researcher

I have accurately read out the information sheet to the participant and to the best of my ability made sure of the following:

- That the participant consent has been given voluntarily and free of duress.
- Refusal to participate or withdraw from the study will not in any way compromise the quality of care and treatment given to the patient.

- All information will be treated with confidentiality
- The results of this study might be published to enhance the knowledge of the subject of research.
- That I have answered all the questions asked by the participant to the best of my ability and knowledge.
- That a copy of this informed consent form has been provided to the participant.

Name of researcher/ person taking consent…….

Signature of researcher/ person taking consent …….

Date……

APPENDIX III CONSENT FORM (SWAHILI VERSION)

FOMU YA MAKUBALIANO YA KUJIUNGA NA UTAFITI

Fomu hii ya makubaliano ni ya wale watoto ambao wanahudumiwa kwenye kliniki ya upasuaji wa watoto katika hospitali ya Kenyatta na wamealikwa kujiunga na utafiti

"**Assessment of vitamin B12 status after ileal resection in paediatric patients managed for intusussception at Kenyatta National Hospital"**

Mtafiti mkuu: Dkt. Leon Onkunya

Kituo: Kitengo cha Upasuaji, Shule ya Afya, Chuo kikuu cha Nairobi.

Fomu hii ya makubaliano ina sehemu tatu:

- Habari itakayo kusaidia kukata kauli
- Fomu ya makubaliano (utakapo weka sahihi)
- Ujumbe kutoka kwa mtafiti

Utapewa makala ya fomu hii.

SEHEMU YA KWANZA: Ukurasa wa habari

Kitambulizi

Jina langu ni Dkt. Leon Onkunya na ninafanya utafiti wa shahada ya juu katika upasuaji wa watoto kwenye chuo kikuu cha Nairobi. Ninafanya utafiti kwa anwani ya "**Assessment of vitamin B12 status after ileal resection in paediatric patients managed for intusussception at Kenyatta National Hospital"**

Lengo Kuu la Utafiti

Wagonjwa wengine ambao wamefanyiwa upasuaji kutokana na intusussception hutolewa sehemu ya mwisho ya ileamu. Hii ndio tovuti ya kunyonya vitamini B12 katika mwili. Kwa hivyo wagonjwa hawa wako katika hatari ya malabsorption ya vitamini B12 na athari ya neva na ya

hematolojia. Idadi na wakati wa upungufu wa vitamini b12 katika wagonjwa kama hao haijulikani katika usanidi wetu.

Ushiriki wa hiari/ haki ya kukataa

Ningependa kukualika katika ushiriki wa utafiti huu. Utapata nafasi ya kuuliza maswali kuhusu utafiti huu, aidha kutoka kwangu au kutoka kwa msaidizi wangu. Baada ya kuelewa kabisa undani wa maelezo ya utafiti, ushiriki wako utakuwa wa hiari. Iwapo utaamua kutoshiriki katika utafiti, hautanyimwa matibabu. Isitoshe, ukishaamua kushiriki, ni haki yako kukataa kuendelea na ushiriki huo wakati wowote ule bila madhara yoyote.

Taadhimu ya siri

Ujumbe wote utakaotokana nawe utahifadhiwa kwa siri, na utatumika tu na wahusika wa utafiti kwa malengo ya utafiti pekee. Jina lako halitaorodheshwa popote katika utafiti huu; nambari spesheli itatumika katika utambulizi wako.

Utumizi wa matokeo ya utafiti

Nakala za matokeo ya utafiti huu zitahifadhiwa kwa siri katika maktaba ya Idara ya Upasuaji, Chuo Kikuu cha Nairobi. Kwa minajili ya kuendeleza ujuzi wa Sayansi ya Utabibu, huenda haja ya kuarifu wauguzi wengine kuhusu utafiti huu itokee. Cha muhimu ni kwamba, ruhusa itaombwa kutoka kwa Afisi ya Maadili ya Utafiti inayosimamia utafiti katika hospitali kuu ya Kenyatta na Chuo Kikuu cha Nairobi, kabla ya kutumia matokeo ya utafiti huu katika warsha za Sayansi au kuyachapisha katika majarida ya Sayansi. Nyakati hizo, ujumbe wa kibinafsi hautafichuliwa kamwe.

Madhara

Utafiti huu hauna madhara yoyote kwako ama kwa mtoto wako.

Gharama/ Malipo

Hakuna gharama ya ziada wala malipo utakayopata kutokana na kushiriki kwako katika utafiti.

Anwani za Wahusika

Ikiwa uko na maswali ungependa kuuliza baadaye, unaweza kuwasiliana na:

1. **Mtafiti Mkuu**

Dkt. Leon Onkunya

Kitengo cha Upasuaji, Shule ya Afya, Chuo Kikuu cha Nairobi,

SLP 19676 KNH, Nairobi 00202.

Simu: 0720955652

2. **Mtafiti Msaidizi**

Dkt. Robert M. Mugo

Kitengo cha Upasuaji, Shule ya Afya, Chuo Kikuu cha Nairobi,

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Simu: 07385491953

3. **Karani**

KNH/ UON-ERC

SLP 20723 KNH, Nairobi 00202

Simu: +254-020-2726300-9 Ext 44355

Barua pepe: KNHplan@Ken.Healthnet.org

4. **Wahadhiri wahusika**

Dkt. Francis Osawa

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Dkt. Peter Mwika

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Simu: 0202726300

Dkt. Swaleh Shahbal

Idara ya Upasuaji, Shule ya Afya, Chuo Kikuu cha Nairobi,

SLP 19676 KNH, Nairobi 00202.

Simu: 0202726300

Dkt. Timothy Jumbi

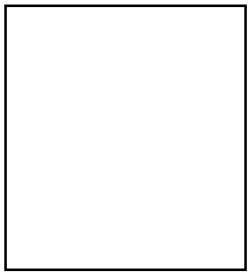
Hopitali Kuu ya Kenyatta,

SLP 19676 KNH, Nairobi 00202.

Simu: 0202726300

SEHEMU YA PILI: Fomu ya makubaliano

Nimeelezwa utafiti huu kwa kina. Nakubali kushiriki utafiti huu kwa hiari yangu. Nimepata wakati wa kuuliza maswali na nimeelewa kuwa iwapo nina maswali zaidi, ninaweza kumuuliza mtafiti mkuu au watafiti waliotajwa hapa juu.



Jina la Mshiriki……..

Sahihi la shahidi/ Alama ya kidole cha mshiriki……

Tarehe……..

Kwa wasioweza kusoma na kuandika:

Nimeshuhudia usomaji na maelezo ya utafiti huu kwa mshiriki. Mshiriki amepewa nafasi ya kuuliza maswali. Nadhibitisha kuwa mshiriki alipeana ruhusa ya kushiriki bila ya kulazimishwa.

Jina la shahidi…….

Sahihi la shahidi…….

Tarehe……

SEHEMU YA TATU: Ujumbe kutoka kwa mtafiti

Nimemsomea mshiriki ujumbe kiwango ninavyoweza na kuhakikisha kuwa mshiriki amefahamu yafuatayo;

- Kutoshiriki au kujitoa kwenye utafiti huu hautadhuru kupata kwake kwa matibabu.
- Ujumbe kuhusu majibu yake yatahifadhiwa kwa siri.
- Matokeo ya utafiti huu yanaweza chapishwa ili kuwezesha kutibu bakteria katika mkojo.

Ninathibitisha kuwa mshiriki alipewa nafasi ya kuuliza maswali na yote yakajibiwa vilivyo.

Ninahakikisha kuwa mshiriki alitoa ruhusa bila kulazimishwa.
Mshiriki amepewa nakala ya hii fomu ya makubaliano.

Jina la mtafiti……..

Sahihi ya mtafiti……

Tarehe……

APPENDIX IV: ASSENT FORM (ENGLISH)

This is for children aged 6-17 years

Study Title: **ASSESSMENT OF VITAMIN B12 STATUS AFTER ILEAL RESECTION IN PAEDIATRIC PATIENTS MANAGED FOR INTUSUSSCEPTION AT KENYATTA NATIONAL HOSPITAL**

Study Site: Kenyatta National Hospital

My name is Dr. Leon Onkunya, a postgraduate student in Pediatric Surgery, Department of Surgery, University of Nairobi. I am conducting a study on the above topic.

If you agree to be part of this study, blood samples will be collected from you and analyzed in our laboratory for vitamin B12 levels.

Participation in this study is voluntary and you will not get any monetary benefit from participation in the study.

When we are finished with this study, we will write a report about what was learned. This report will not include your name or that you were in the study.

You don't have to be in this study if you don't want to be. If you decide to stop after we begin, that is okay. Your parents will know about the study too.

If you decide you want to be in the study, please sign your name

Name……Signature……

Date…….

Name of Parent or Guardian…….

Statement by researcher

I have read the information to the participant and to the best of my ability made sure that the participant understands what the study entails.

A copy of this assent has been provided to the parents/ relative.

Name…….

Signature ……

Date……

APPENDIX V: ASSENT FORM (SWAHILI)

ASSENT FORM (SWAHILI)

FOMU YA IDHINI YA WATOTO WALIO NA UMRI WA MIAKA SITA HADI KUMI NA SABA.

Jina langu ni Dkt. Leon Onkunya. Mimi ni daktari ninayesomea upasuaji katika Chuo Kikuu cha Nairobi. Ninafanya utafiti kwa anwani ya, "**ASSESSMENT OF VITAMIN B12 STATUS AFTER ILEAL RESECTION IN PAEDIATRIC PATIENTS MANAGED FOR INTUSUSSCEPTION AT KENYATTA NATIONAL HOSPITAL"**

Ukikubali kushiriki katika utafiti huu, kipimo cha damu yako kitafanywa katika maabara la hospitali kuu ya Kenyatta ili kuchunguza kiwango cha vitamin B12.

Kushiriki katika utafiti huu ni kwa hiari yako na hamna masharti yeyote ya lazima. Una haki ya kujiondoa kutoka ushiriki wa utafiti huu wakati wowote upendavyo na uamuzi huo hauwezi dhuru matibabu yako kwa vyovyote vile.

Hakuna hatari wala gharama ya ziada yeyote itakayo kukumba kutokana na kushiriki katika utafiti huu.

Tutakapo maliza utafiti huu, tutaandika ripoti kuhusu tulilojifunza. Hakuna popote pale nitakapotaja jina lako. Hivyo basi hamna atakaye tambua kwa majina walioshiriki.

Mzazi au mlezi wako atajulishwa kuhusu utafiti huu pia.

Nitakupa nakala ya fomu hii ukikubali kushiriki katika utafiti huu.

Kama umekubali kushiriki katika utafiti:

Jina lako……..

Sahihi yako ……..

Tarehe ……

Jina la Mzazi au Mlezi…….

Mtafiti aliyekupa maelezo ya utafiti

Jina …….

Sahihi ……

Tarehe…….

APPENDIX 6: BUDGET

Particulars	**Amount (Ksh)**
Research fee for KNH- ERC	5,000
Statistician	30,000
Stationery	5,000
Printing and binding	5,000
Research assistant	25,000
Vitamin B12 assays	252,000
Total	322,000
Miscellaneous 10% of total	32,200
GRAND TOTAL	**354,200**

APPENDIX 7: DATA COLLECTION FORM

A

1. Patient identification number _____
2. Date of birth _____
3. Sex _____
4. Residence _____

B

1. Current age _____
2. Age at surgery _____
3. Duration post-surgery (months) _____

C

Vitamin B12 levels pg/ml

◯ Normal (>163 pg/ml)

◯ Borderline (109-163 pg/ml)

◯ Low (< 109 pg/ ml)

D

Vitamin B12 deficiency

Yes ☐ No ☐

E CLINICAL MANIFESTATIONS OF VITAMIN B12 DEFICIENCY

Hyperpigmentation	PRESENT	ABSENT
Jaundice	PRESENT	ABSENT
Vitiligo	PRESENT	ABSENT
Glossitis	PRESENT	ABSENT
Gait abnormality	PRESENT	ABSENT

Seizures PRESENT ABSENT

Others ……..

Haemoglobin level g/dl mean corpuscular volume fL

White Blood Cell count \9/L

Platelet count \9/L