THE EFFECT OF A FORTIFIED FOOD, E'PAP, ON ORAL CANDIDIASIS IN ADULT TB PATIENTS ATTENDING CLINICS IN ALEXANDRA, JOHANNESBURG, SOUTH-AFRICA

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Master of Science in Epidemiology and Biostatics

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TABLE OF CONTENTS

DECLARATION

I, U Wai Lin Phyo declare that this research report for the degree of Masters of Science in Epidemiology and Biostatistics is my own work except as indicated in the references and acknowledgements. It has not been submitted by myself or anyone else for a degree at this or any other university. The materials consulted have been acknowledged.

The University of the Witwatersrand Human Research Ethics Committee approved the study (Clearance Certificate number M120723).

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26/May/2014

DEDICATION

This research report is affectionately dedicated to my parents, U Htein Lin and Daw Yin Yin Htay for their love, support and encouragement.

ABSTRACT

Introduction

The association between tuberculosis (TB) and malnutrition is well known. Malnutrition also weakens the immune system increasing the chance of latent TB progressing to active disease. Nutritional interventions can help improve overall quality of life and can reduce susceptibility to opportunistic infections including all forms of Oral Candidiasis (OC) which includes: (1) pseudomembranous candidiasis (oral thrush), (2) atrophic (erythematous) candidiasis, (3) hyperplastic candidiasis, and (4) angular cheilitis. This secondary data analysis of a longitudinal follow-up study evaluates the impact of a fortified supplementary food on OC among adult TB patients over a three month period.

Results

At baseline, an overall prevalence of 33% of OC (27 out of 83) was found in 83 adult TB patients; (pseudo-membranous 46% (16 out of 35), erythematous 26% (9 out 35), angular chelitis 20% (7 out 35) and hyperplastic 8% (3 out of 35). Thirty five different types of OC were found in 27 of the subjects some of whom manifested with more than one type of OC. Almost 89% of these TB patients had low levels of malnutrition (8% for selenium, 55% for iron, 62% for Vit-A, 42% for albumin, 47% for Vit-D and 34% for zinc). Their p values related to OC were (p=0.64 for selenium, p=0.74 for iron, p=0.19 for Vit-A, p=1 for albumin, p=1 for Vit-D and p=0.09 for zinc) showing no statistically significant difference for malnutrition in each different type of micronutrient related to OC at baseline. However, there was a statistically significant difference in HIV status (p=0.01) related to OC among factors such as sex (p=0.34), employment status (p=0.74), ARV status (p=0.46) and wellbeing (p=0.18) at baseline. OC was statistically significant at both 2nd and 3rd visits using univariate analysis p=0.04 (95%CI 0.22 to 0.97) and p=0.00 (95%CI 0.06 to 0.43) and also multivariate analysis p=0.01(95%CI 0.17 to 0.85) and p=0.00 (95%CI 0.04 to 0.34) with reference to the 1st visit (the prevalence of OC was significantly decreased in both 2nd and 3rd visits). For different types of clinical OC, pseudomembranous candidiasis was the only type of OC that showed statistically significant difference at the 3rd visit in both univariate analysis (p= 0.01, 95%CI 0.01 to 0.46) and multivariate analysis (p= 0.00, 95%CI 0.01 to 0.38) with reference to 1st visit.

Discussion and Conclusions

This study found no significant association between overall micronutrient level and the presence of OC at baseline. However, micronutrient interventions to the 83 adult TB patients receiving treatment at Johannesburg city clinics located in Alexandra showed a decrease in prevalence of different types of OC in both 2^{nd} and 3^{rd} visits. This analysis showed encouraging results which indicated a beneficial effect of e'Pap in adult TB patients.

ACKNOWLEDGEMENTS

I wish to express my thanks to my supervisors (Prof. Michael Rudolph and Dr. Edmore Marinda) and also Dr. Margaret Urban. They offered advice on the theme of the report, analysis, organization and writing. This report would not have been made possible without their support and encouragement.

FIGURES

TABLES

DEFINITIONS

e'Pap : e'Pap is a precooked maize meal and soya based food containing 28 nutrients in a bio-available form. It is manufactured by Econocom Foods of Johannesburg, South Africa.

TB: Tuberculosis is a common infectious disease generally affecting the lungs caused by *Mycobacterium tuberculosis*, a pathogenic bacterium.

OC: Oral candidiasis is an infection of the oral cavity caused by the yeast *Candidia albicans*; which presents in the following forms: oral thrush (pseudomembranous candidiasis), erythematous candidiasis, hyperplastic candidiasis and angular cheilitis.

ACRONYMS AND ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
ARV	Anti-retroviral (class of drugs used to treat HIV infection)
BMI	Body Mass Index (kg/m^2)
CD4	Sub-class of T-helper lymphocytes, expressed as number per cubic millimeter of blood
Fe	Iron
HIV	Human immunodeficiency virus
K	Potassium
MTB	*Mycobacterium tuberculosis*
MDR TB	Multi drug resistant tuberculosis
NHLS	National Health Laboratory Services
OC	Oral Candidiasis
SA	South Africa
Se	Selenium
TB	Tuberculosis
TLC	Themba Lethu Clinic
ug/l	Microgram per liter
UNAIDS	Joint United Nations Programme on HIV/AIDS
Vit	Vitamin
Vit-A	Vitamin A
Vit-B	Vitamin B
Vit-B2	Vitamin B2 (Riboflavin)
Vit-C	Vitamin C
Vit D	Vitamin D
VD_3	Vitamin D_3
Vit-E	Vitamin E
WHO	World Health Organization
WITS	University of the Witwatersrand
Zn	Zinc

CHAPTER 1: INTRODUCTION

1.1 Background

Micronutrients play a key role in disease prevention in young adults and older people [1]. Micronutrients are vitamins and minerals essential for health but are only required in minute amounts. Nutritional deficiency (malnutrition) is defined as an imbalance of nutrients which is caused by either an unbalanced intake of nutrients or an inadequate intake of nutrients [1, 2]. There are many causes of malnutrition and there is no clear distinction between age-related and pathological deficiencies [3]. Poverty, mal-absorption, poor oral health, loss of appetite, illness, disability, false dietary beliefs, depression, and cognitive impairment are some of the reasons mentioned as causes of malnutrition [3,4].

Several studies have shown that nutrient intake, quality of diet and general health are determined by multiple factors including oral health. There is a relationship between nutritional status and oral health in older people [4,5]. Oral conditions in older age groups may be related to deficient nutrient intake and nutritional status [6]. Oral candidiasis (OC), which includes pseudomembranous candidiasis, erythematous candidiasis, hyperplastic candidiasis and angular cheilitis, has been found to be associated with malnutrition and has a negative effect on energy intake which may further aggravate nutritional status [7].

It is estimated that one-third of the world's population is infected with *Mycobacterium tuberculosis* (MTB) [8]. Tuberculosis (TB) caused by MTB is a major cause of morbidity and mortality in developing countries [8,9]. About 11% of the world's population lives in Africa, but the continent accounts for about 30% of all MTB-infected subjects in the world [9]. The TB rate has increased in South Africa (SA) over the last 20 years and it now has the third-highest in the world [10]. TB is the most common opportunistic infection among South African HIV-infected patients who remain at high risk for TB throughout their lives. Diagnosis of drug-resistant TB remains a challenge in SA [11, 12]. HIV-TB co-infected patients have a higher frequency of smear negative TB sputum tests and are four times more likely to have extra-pulmonary TB than their HIV negative counterparts [13]. In addition, the outcome for TB treatment depends on a well-functioning cell-mediated immune system [14].

Several studies have reported specific micronutrient deficiencies in TB patients and TB infection also affects overall nutritional status [15]. Micronutrient supplements may be an effective and safe method of reducing the burden of TB/HIV co-infection [16].

e'Pap is a precooked maize meal and soya based food containing 28 nutrients in a bio-available form [17]. Vitamin and nutrient enriched foods can be vital for individuals suffering from illnesses and has been shown to decrease mortality [16, 18].

The three main strategies widely used to combat micronutrient deficiencies are food diversification, food fortification, and the consumption of medicinal supplements. Food fortification generally refers to the addition of micronutrients to food-stuffs [19, 20]. It is a cost-effective public health intervention which can provide rapid improvement in the micronutrient status of individuals or targeted populations. It needs to be supported by adequate food regulations and labeling, quality assurance and monitoring to ensure correct use and the desired outcome [20, 21]. The South African Medical Research Council assembled a group of experts to study all aspects of food fortification in South Africa in 1976 following which the fortification of maize meal with riboflavin (Vit-B2), folic acid and nicotinic acid were recommended [19] and the Department of Health of South Africa embarked on a fortification programme of maize meal as part of a multipronged approach to alleviate malnutrition in 2003 [22]. There are many variables that affect the positive health benefits of food fortification but challenges remain in terms of technical and managerial capacity constraints, the need for systematic compliance with procurement specifications and quality control, clearer policies on micronutrient content labeling, and the need for cash resources to support many aspects associated with local processing and fortification activities [23].

1.2 Problem Identification

1.2.1 Malnutrition and Oral Health- The association between malnutrition and poor oral health problems has been studied in recent years because of the impact that these problems can have on the health system as well as on individuals [24]. Poor nutritional health is often associated with poor oral health and vice versa [25]. Reduced salivary secretion and a feeling of oral dryness in older age could have a negative effect on nourishment, appetite and oral comfort. Both malnutrition and decreased salivary flow may also be associated with medical disorders and their medication [26,

27]. OC is a common problem among people who wear dentures because it can be difficult to keep dentures clean due to dryness of the mouth (Xerostomia) [28]. OC is also common in people with diabetes [28,29].

1.2.2 Malnutrition and HIV/TB co-infection- In parts of southern Africa, people living on or below the poverty line are at risk of micro-nutrient deficiency as they consume a diet consisting mainly of refined maize meal which does not contain adequate amounts of fat, vitamins or minerals, which may be lost during the refining process [30]. Additionally micro-nutrient deficiencies have been reported in individuals with tuberculosis and in those with HIV infection. The increase in TB cases in South Africa in recent years is related to multiple factors including the breakdown of TB control programmes, drug and multidrug resistant TB strains, and concomitant HIV infection. One third of 40 million people living with HIV/ AIDS is also infected with *Mycobacterium tuberculosis* [31,32].

1.3 Study Objective

This study aimed to investigate whether three months of dietary supplementation (e'Pap) given to adult TB patients would improve or reduce the occurrence of oral candidiasis.

1.3.1 Expected Outputs:

1. Quantification of socio-demographic characteristics of adult TB patients participating in a micro-nutrient supplementation program and prevalence of oral candidiasis among them.
2. Quantification of levels of micro-nutrient deficiency (selenium, iron, zinc, vitamin A and Vitamin D) including albumin among these patients prior to during and after nutritional intervention.
3. Assessment of the efficacy of the supplementation with e'Pap on oral candidiasis while accounting for other factors including age, sex, HIV status, ARVs and Body Mass Index (BMI).

1.3.2 Null Hypothesis: There is no change in the prevalence of oral candidiasis in adult TB patients after a three-month nutritional supplementation with e'Pap.

1.3.3 Alternative Hypothesis: There is a decline in the prevalence of oral candidiasis in adult TB patients after a three-month nutritional supplementation with e'Pap.

CHAPTER 2: LITERATURE REVIEW

2.1 Nutrition (micronutrients) and Oral Health- Many published studies link specific micro-nutrient deficiencies to oral health impairment. Oral health impairment is associated with nutritional deficit which could be reduced by greater integration between dentistry and nutritional health promotion for older adults [33]. Selenium (Se) has both beneficial and harmful effects depending on dose [34]. When combined with vitamin E (Vit-E), it works as an antioxidant by scavenging damaging particles, free radicals, in the body. It is needed for the immune system to work properly and is also important in prevention of oral cancer [34, 35]. Albumin is the main protein of plasma and its main function is to regulate the colloidal osmotic pressure of blood [36]. Vit-A can prevent oral leukoplakia [37]. Beta-carotene and cis-retinoic acid are also important in preventing precancerous lesions such as mucosal dysplasia in head and neck region [38]. In healthy people who have been exposed to tuberculosis, a single oral dose of vitamin D (Vit-D) enhances their immunity to the MTB infection [39]. It was found experimentally that systemic vitamin D_3 (VD_3) treatment significantly inhibited neoplastic transformation in the hamster buccal pouch [40]. Oral mucosal changes and atrophic changes of the tongue were found in iron deficient anemic individuals in an age- and sex-matched hospital case control study among Sri Lankan females [41]. Reduced micronutrient intake (Vit A, C & E and Se & Zn) has also been associated with impaired overall immunity [42]. Thus, it appears that nutrition interventions can assist people living with TB and HIV to improve their nutritional status and thus better manage symptoms, reduce susceptibility to opportunistic infections such as candidiasis, promote response to medical treatment, and improve overall quality of life [42, 43].

2.2 Oral Manifestations associated with HIV- There are five main groups of oral manifestations associated with HIV infection: fungal, viral, bacterial, neoplastic and others. Oral candidiasis (OC) is one of the most common oral lesions and can be grouped into (1) candidiasis (oral thrush), (2) atrophic (erythematous) candidiasis, (3) hyperplastic candidiasis, and (4) angular cheilitis [44,45]. Oral thrush is caused by the overgrowth or infection of the oral cavity by the yeast like fungus, *candida albicans*. It manifests as white, cream-coloured, or yellow plaques mostly on the cheek mucosa but also can be found on the tongue, palate, gum, floor of the mouth, and lips. The mucosa may appear red when the plaque is removed [44,45,46]. Hyperplastic candidiasis is characterized by white plaques which cannot be removed by scraping. Their most common location is the cheek

mucosa and most often is found in the lip commissures in HIV patients [47, 48]. The erythematous (atrophic) type is characterized by a reddish appearance of variable colour intensity[49]. Common locations are the palate and dorsal surface of the tongue, followed by the cheek mucosa [49,50]. Angular cheilitis is characterized by cracks radiating from the angles of the mouth, often associated with small white plaques [45, 51].

Research carried out in India in 2010 showed that the prevalence of oral lesions in HIV positive patients was 76.7% (n = 306). OC was found among almost 40% (157) of the 369 patients who were HIV positive and it was also found to be significantly associated with a reduced CD4 cell count, (P = 0.000, Odds ratio = 3.1; 95% Confidence interval 1.9-4.9) comparing CD4 counts below 200 and above 200 cells/mm^3 [52].

A cross-sectional analytic study for adults patients attending the Khutsong and Heidelberg public health care facilities in Johannesburg, South Africa in 2005 showed that pseudomembranous candidiasis 80(38%), erythematous candidiasis 50(24%) and angular cheilitis 12(6%) were found among HIV-positive patients (n=210) [64].

A retrospective analysis of existing data collected from a large urban cohort of over 16,000 HIV infected adults who started ARV at Themba Lethu Clinic (TLC) in Johannesburg, South Africa 2011/12 showed the prevalence of OC (18%) [65].

Based on the literature review, oral thrush (pseudomembraneous candidiasis) is one of the commonest oral candidiasis and occurs commonly among people with HIV especially those with low CD4 cell counts [44,45,52]. Patients who have HIV/AIDS and TB co-infections are more susceptible to oral candidiasis, compared to persons solely infected with HIV [43, 45].

2.3 TB/HIV co-infection and Oral Candidiasis- Tuberculosis (TB) is a major public health problem in South Africa and is the leading cause of death among people who are HIV-positive [9,53]. The high prevalence of multi-drug resistant TB (MDR TB) in South Africa underscores the importance of effective treatment programs for drug-resistant TB. TB remains a major clinical challenge, particularly in patients with HIV co-infection which also complicates TB therapy [9, 54,

55]. HIV and TB form a lethal combination, each speeding the progress of the other. People who are living with HIV and who are also infected with TB are more susceptible to secondary bacterial and fungal infections such as oral candidiasis (OC), compared to people solely infected with HIV [53, 56].

CHAPTER 3: METHODS

3.1 Study Design – This is the secondary data analysis of previously collected data from a nutritional intervention study (A pilot study assessing the impact of a fortified supplementary food on the health and well-being of Cre`che children and adult TB patients in South Africa published in January, 2013). This study was conducted between September and December 2011. Nutritional status derived from selenium, albumin, zinc, iron, vitamin A and vitamins D as well as oral conditions were assessed at recruitment among adult TB patients (n=83). Patients were provided with 100g daily of a fortified maize meal based product (e'Pap) and levels of micro-nutrients and the status of oral conditions were assessed at baseline (1st visit). They were asked to return for 2 subsequent data collection visits (2nd and 3rd visits), between 4-6 weeks apart between September and December 2010.

3.2 Study Population- Study participants were 83 adult patients (male and female) receiving TB treatment at Johannesburg City clinics located in Alexandra, Johannesburg, South Africa. This comprised all the adults being treated for TB at these clinics.

3.3 Inclusion Criteria

The study subjects were adult male and female patients (18-60 years of age) receiving TB care and treatment at Johannesburg city clinics located in Alexandra who gave informed consent to participate in the primary study. They also agreed to visit the clinic for follow-up assessments.

3.4 Data Collection

The current analysis made use of the following information collected during the primary study;

1. A questionnaire which captured baseline demographic data.
2. A clinical assessment form which captured HIV status, anthropometric measurements, blood plasma indices and clinical signs of nutritional deficiency.
3. Results from tests of venous blood specimens which were collected by a qualified and experienced nurse from all study participants at each study visit and analysed by the National Health Laboratory Services (NHLS) at University of the Witwatersrand (WITS).
4. Oral examination results were carried out and recorded by two calibrated oral health clinicians.

3.5 Selected Variables

The following variable values were extracted from the primary data set**:**

Socio-demographic and HIV related - age, sex, marital status, employment status, household size, well-being status, alcohol use, tobacco use HIV status, ARV use and CD4 counts

Nutritional indicator variables for e'Pap efficacy- Selenium, Iron, Zinc, Albumin, Vitamin A and Vitamin D

Outcome variable – presence or absence of oral candidiasis (pseudo-membranous candidiasis, erythematous candidiasis, angular cheilitis and hyperplastic candidiasis)

3.6 Data Processing and analysis

The primary data set was carefully checked to identify any obvious data entry errors or values outside of expected ranges. Data errors can strongly influence and bias the results and hence were detected and corrected by listing values of all variables as well as examining the relationships between variables. The source documents were consulted when any missing values were found. Following cleaning the data set was transferred to STATA11 for analysis. Age, BMI and nutritional levels (Selenium, Iron, Zinc, Albumin, Vitamin D, and Vitamin A) were continuous variables in the source data set; for the purpose of this assessment they were transformed into categorical variables in accordance with the stated objectives.

For the 1st objective of the study (quantification of socio-demographic characteristics of adult TB patients participating in a micro-nutrient supplementation program and prevalence of oral candidiasis among them), cross tabulation (Fisher's exact test n<5 per cell) was used to describe frequencies and percentages of outcome related to exposure.

For the 2nd objective of quantification the levels of micro-nutrient deficiency (selenium, albumin, iron, zinc, vitamin A and Vitamin D) among adult TB patients prior to during and after nutritional intervention, those micronutrients continuous variables from primary data were transformed into categorical variables and cross tabulation (Fisher's Exact test n < 5 per cell) was used to describe frequencies and percentages of micronutrients related to exposure. The following normal micronutrient levels outlined in **Table 1** are used by the NHLS based on Tietz Clinical Guide to Laboratory Tests, 4th edition [57].

Table 1: International normal ranges for micronutrients including albumin (Tietz Clinical Guide to Laboratory Tests, 4th edition)

Micronutrients	**Adult Normal Range**
Selenium	46 – 143 µg/L
Iron	Male (11.6 – 31.3 µmol/L) Female (9 – 30.4 µmol/L)
Zinc	8.2 – 23 µmol/L
Vitamin D	49 – 172 nmol/L
Vitamin A	1.05 – 2.80 µmol/L

Albumin	35-52g/L

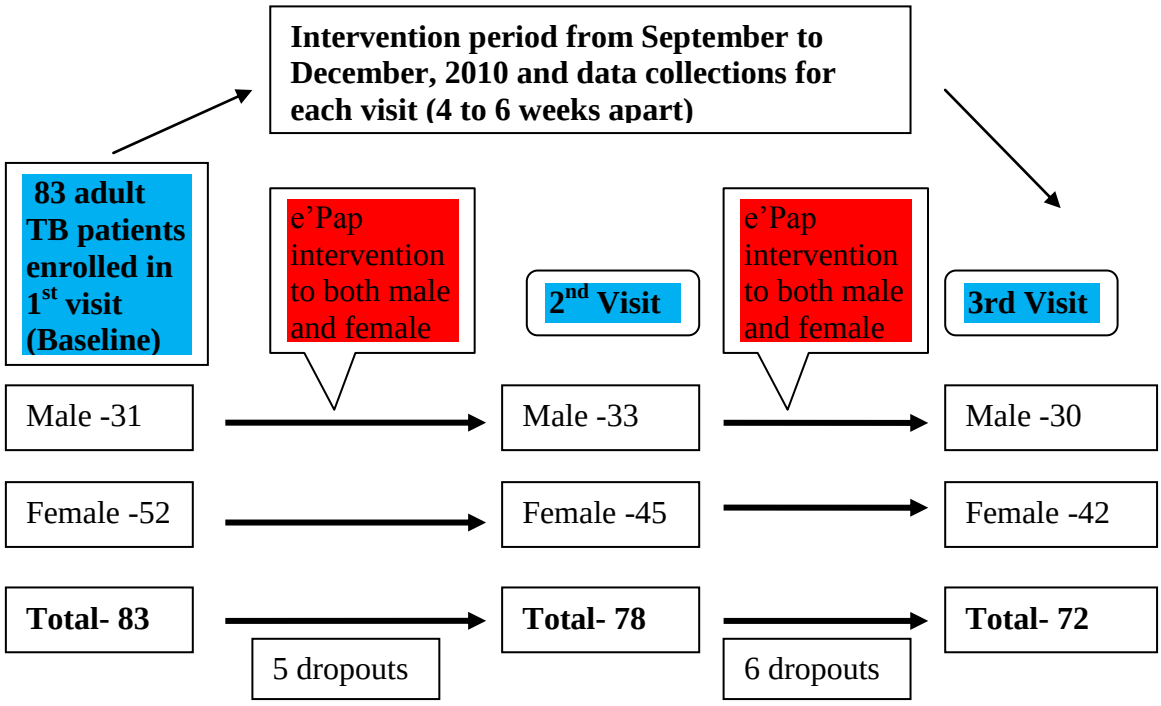
For the 3rd objective (assessment of the efficacy of the supplementation with e'Pap on oral candidiasis while accounting for other factors including age, sex, HIV status, and Body Mass Index (BMI)), simple logistic regression and multiple logistic regressions were used for outcome of OC (Yes/No) related with other factors to assess the efficacy of micro-nutrients on oral candidiasis accounting for other factors such as age, sex, HIV status, socio-demographics and anthropometric measurements. Baseline data was used as a reference and odd ratios, p-values, 95% CI which were also used for interpretation of 2nd and 3rd visits with a relative to 1st visit (baseline).

3.7 Confidentiality

It was found that all participants in the study were assigned unique identifiers and all personal identifiers were removed to maintain confidentiality before any secondary data analysis took place. The ethical clearance for the secondary data analysis was obtained from the Human Research Ethics Committee (Medical) at the University of the Witwatersrand, certificate number M120723 (Appendix F).

CHAPTER 4: RESULTS

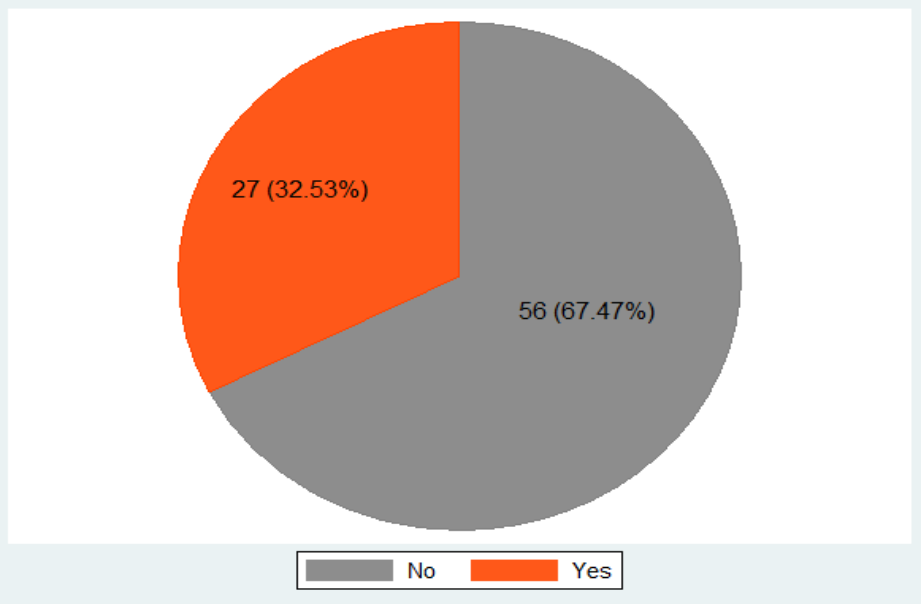
Figure 1: Flow chart for nutritional intervention to adult TB patients (n=83)



Baseline characteristics

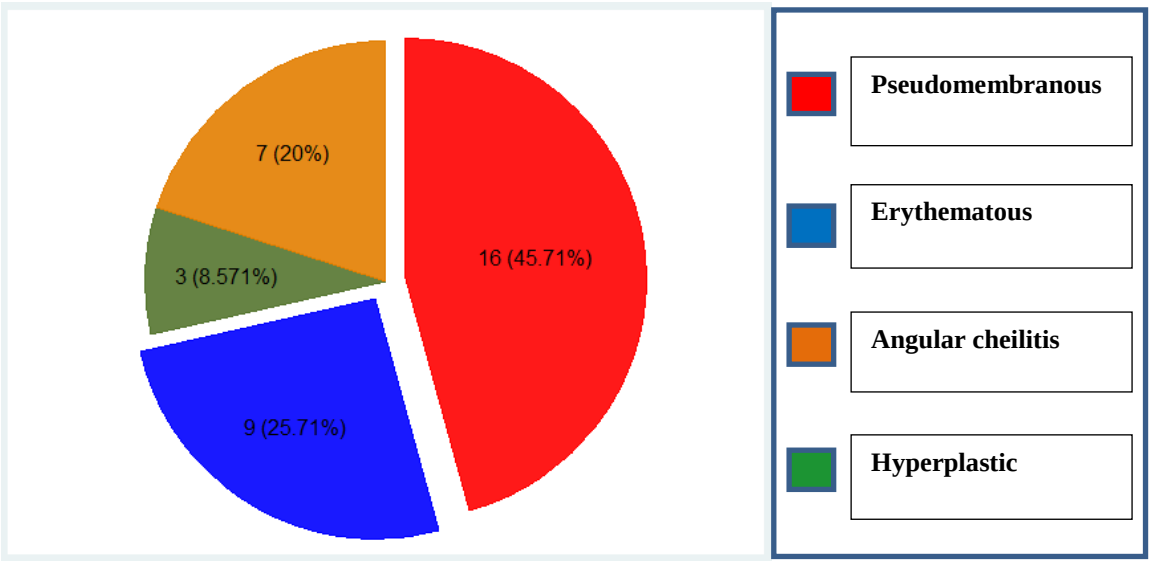
The following 2-D pie charts (**Figures 2** and **3**) showed the prevalence of OC and their different clinical types among TB patient enrolled in 1st visit. Nearly 33% of them had OC and pseudo-membranous candidiasis (46%), erythematous candidiasis (26%), angular cheilitis (20%) and hyperplastic candidiasis (8%) were also found among adult TB patients. Different kinds of OC (pseudo-membranous / erythematous candidiasis and angular cheilitis) were found together in some patients.

Figure 2: Prevalence of Oral Candidiasis (OC) among adult TB patients at baseline (n=27)



** OC (27) includes both one clinical type and combination of different types (e.g pseudo-membranous / erythematous candidiasis and angular cheilitis)**

Figure 3: Prevalence of Oral Candidiasis (OC) by clinical types at baseline (n=35)



Total number of different types of OC was 35 which were found in 27 of subjects some of whom manigested with more than one type of OC (e.g pseudo-membranous/erythematous candidiasis and angular cheilitis found together in some patients)

Table2 shows the baseline characteristics of the 83 adult TB patients included in the study both as a single group and divided into those with OC and without OC.

Sixty three percent of the groups were females, 40% with a recorded age of 31 to 40 and only 26% in employment. Less than 5% of study subjects reported use of alcohol, tobacco or cannabis (dagga).

Sixty-eight percent (n=56) of 82 with known status were HIV positive; of these 57 were taking anti-retroviral medicines (ARVs). The majority (94%) of the studied TB patients described their wellbeing as poor.

HIV status is the only one recorded characteristics which showed statistically significant differences between those with OC compared to those without (p=0.01). Fewer TB patients with OC were HIV negative (7% vs 67%) and nobody reported satisfactory wellbeing.

Table 2: Socio-demographic characteristics of adult TB patients (N=83) associated with OC in an e'Pap study

Variables	Total (N) and percentage (%)	Oral Candidiasis (OC)		p value
		Yes N=27 (33%)	No N=56 (67%)	
Sex	**N=83**	**N=27 (33%)**	**N=56 (67%)**	
Male	N=31 (37%)	N=8 (30%)	N=23 (41%)	**0.34**
Female	N=52 (63%)	N=19 (70%)	N=33 (59%)	
Age	**N=83**	**N=27 (33%)**	**N=56 (67%)**	
Age (in years) 18 to 30	N=24 (29%)	N=6 (22%)	N=18 (32%)	**0.64**
Age (in years) 31 to 40	N=33 (40%)	N=12 (45%)	N=21 (38%)	
Age (in years) 41 to Max	N=26 (31%)	N=9 (33%)	N=17 (30%)	
Employment	**N=80**	**N=27 (34%)**	**N=53 (66%)**	
Yes	N=21 (26%)	N=6 (22%)	N=15 (28%)	
No	N=58 (73%)	N=21 (78%)	N=37 (70%)	**0.74**
Sometimes	N=1 (1%)	N=0	N=1 (2%)	
Missing	N=3			
HIV Status	**N=82**	**N=27 (33%)**	**N=55 (67%)**	
Positive	N=56 (68%)	N=18 (67%)	N=38 (69%)	
Negative	N=16 (20%)	N=2 (7%)	N=14 (26%)	**0.01 *****
Unknown	N=10 (12%)	N=7 (26%)	N=3 (5%)	
Missing	N=1			

ARV Status	**N=83**	**N=27 (33%)**	**N=56 (67%)**	
Yes	N=57 (69%)	N=10 (37%)	N=16 (29%)	**0.46**
No	N=26 (31%)	N=17 (63%)	N=40 (71%)	
Wellbeing	**N=79**	**N=27 (34%)**	**N=52 (66%)**	
Good	N=4 (5%)	N=3 (11%)	N=1 (2%)	
Satisfactory	N=1 (1%)	N=0	N=1 (2%)	**0.18**
Poor	N=74 (94%)	N=24 (89%)	N=50 (96%)	
Missing	N=4			
BMI	**N=79**	**N=24 (30%)**	**N=55 (70%)**	
Underweight	N=22 (28%)	N=10 (42%)	N=12 (22%)	
Normalweight	N=38 (48%)	N=10 (42%)	N=28 (51%)	**0.36**
Overweight	N=12 (15%)	N=3 (12%)	N=9 (16%)	
Obese	N=7 (9%)	N=1 (4%)	N=6 (11%)	
Missing	N=4			
Alcohol	**N=83**	**N=27 (33%)**	**N=56 (67%)**	
None	N=78 (94%)	N=26 (96%)	N=52 (92%)	
Once a week	N=3 (4%)	N=1 (4%)	N=2 (4%)	**1.00**
Everyday	N=1 (1%)	N=0	N=1 (2%)	
Undisclosed	N=1 (1%)	N=0	N=1 (2%)	
Cannibis (Dagga)	**N=82**	**N=27 (33%)**	**N=55 (67%)**	
None	N=82 (100%)	N=27 (100%)	N=55 (100%)	
Missing	N=1			
Tobacco	**N=83**	**N=26 (32%)**	**N=56 (68%)**	
None	N=78 (96%)	N=23 (88%)	N=55 (98%)	
Once week	N=1 (1%)	N=1 (4%)	N=0	**0.09**
Everyday	N=2 (2%)	N=1 (4%)	N=1 (2%)	
Undisclosed	N=1 (1%)	N=1 (4%)	N=0	
Missing	N=1			

**Fisher's Exact test (n < 5 per cell) was used for categorical variables. p value for each variable related with OC **

Table 3 below looks at each of the selected micronutrients (Selenium, Iron, Zinc, Vitamin D, and Vitamin A) including albumin and how many of the TB patients with and without OC had normal levels or low levels of each. Although albumin is not a micronutrient, it is included here as a general measure of nutritional status. The data was available as a continuous variable which was reclassified into normal, low and high values using the guidelines in **Table 1**.

Table 3: Different levels of micronutrients variables (selenium, iron, zinc, vitamin A and vitamin D) and albumin among adult TB patients (N=83) associated with OC in an e'Pap study

Variables	Total (N) and percentage (%)	Oral Candidiasis (OC)		p value
		Yes N=27 (33%)	No N=56 (67%)	
Selenium	**N=37**	**N=8 (22%)**	**N=29 (78%)**	
Male	N=18	N=4	N=14	
Low	N=2 (5%)	N=1 (13%)	N=1 (3%)	
Normal	N=16 (43%)	N=3 (37%)	N=13 (46%)	**0.64**
Female	N= 19	N= 4	N=15	
Low	N=1 (3%)	N=0	N=1 (3%)	
Normal	N=18 (49%)	N=4 (50%)	N=14 (48%)	
Missing	N=46			
Iron	**N=47**	**N=11 (23%)**	**N=36 (77%)**	
Male	N=21	N=5	N=16	
Low	N=12 (25%)	N=3 (27%)	N=9 (25%)	
Normal	N=9 (20%)	N=2 (18%)	N=7 (20%)	**0.74**
Female	N=26	N= 6	N=20	
Low	N=14 (30%)	N=2 (18%)	N=12 (33%)	
Normal	N=12 (25%)	N=4 (37%)	N=8 (22%)	
Missing	N=36			
Zinc	**N=41**	**N=9 (22%)**	**N=32 (78%)**	
Male	N=19	N=4	N=15	
Low	N=6 (15%)	N=3 (34%)	N=3 (9%)	
Normal	N=13 (32%)	N=1 (11%)	N=12 (38%)	**0.09**
Female	N=22	N=5	N=17	
Low	N=8 (19%)	N=2 (22%)	N=6 (19%)	
Normal	N=13 (32%)	N=2 (22%)	N=11 (34%)	
High	N=1 (2%)	N=1 (11%)	N=0	

Missing	N=42			
Albumin	**N=47**	**N=11 (23%)**	**N=36 (77%)**	
Male	N=21	N=5	N=16	
Low	N=11 (23%)	N=3 (28%)	N=8 (22%)	
Normal	N=10 (22%)	N=2 (18%)	N=8 (22%)	**1.00**
Female	N=26	N=6	N=20	
Low	N=9 (19%)	N=2 (18%)	N=7 (19%)	
Normal	N=17 (36%)	N=4 (36%)	N=13 (37%)	
Missing	N=36			
Vitamin D	**N=42**	**N=8**	**N=34**	
Male	N=18	N=3	N=15	
Low	N=11 (26%)	N=2 (25%)	N=9 (26%)	
Normal	N=7 (17%)	N=1 (13%)	N=6 (18%)	
Female	N=24	N=5	N=19	**1.00**
Low	N=9 (21%)	N=2 (25%)	N=7 (21%)	
Normal	N=15 (36%)	N=3 (37%)	N=12 (35%)	
Missing	N=41			
Vitamin A	**N=45**	**N=11**	**N=34**	
Male	N=21	N=5	N=16	
Low	N=15 (33%)	N=4 (36%)	N=11 (32%)	
Normal	N=6 (13%)	N=1 (9%)	N=5 (15%)	**0.19**
Female	N=24	N=6	N=18	
Low	N=13 (29%)	N=1 (9%)	N=12 (35%)	
Normal	N=11 (25%)	N=5 (46%)	N=6 (18%)	
Missing (Total)	N=38			
Micronutrients and albumin	**N=47**	**N=11**	**N=36**	
Male	N=21	N=5	N=16	
Malnutrition	N=19 (41%)	N=5 (45%)	N=14 (38%)	
No malnutrition	N=2 (4%)	N=0	N=2 (6%)	**1.00**
Female	N=26	N=6	N=20	
Malnutrition	N=23 (49%)	N=5 (45%)	N=18 (50%)	
No malnutrition	N=3 (6%)	N=1 (10%)	N=2 (6%)	
Missing (Total)	N=36			

** Fisher's Exact test (n < 5 per cell) was used for categorical variables. p value for each variable related with OC **

** Malnutrition (Below the normal values described in **Table 1**) **

** No malnutrition (Normal and above values described in **Table 1**) **

The following 3-D bar charts (**Figures 4**, **5**, **6**, **7** and **8**) show nutritional status among adult TB patients in relation to several relevant factors (sex, employment status, HIV status, ARV status, and well-being) at baseline. Malnutrition was found to be nearly 10 times higher in both adult TB patients who were unemployed and also in a poor state of well-being as shown in **Figures 5 and 8**.

Figure 4

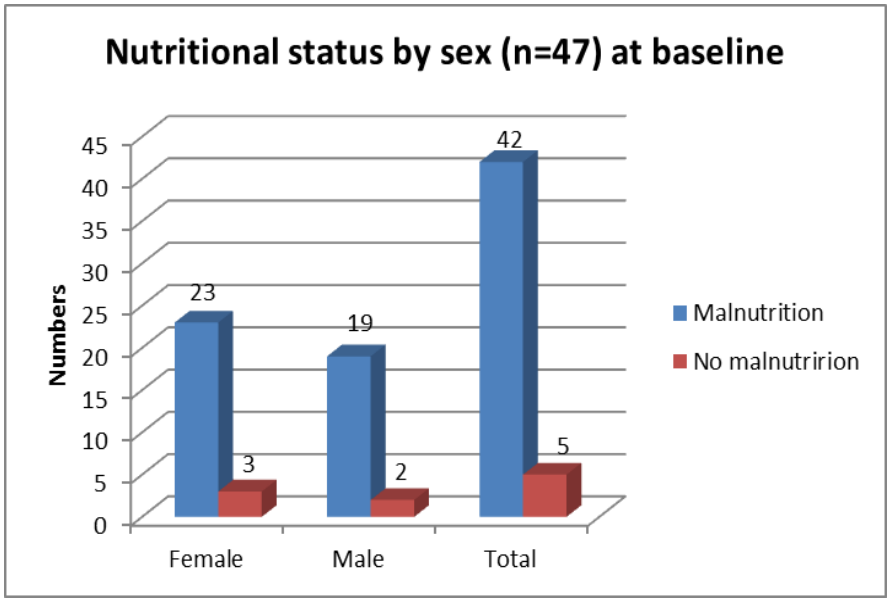


Figure 5

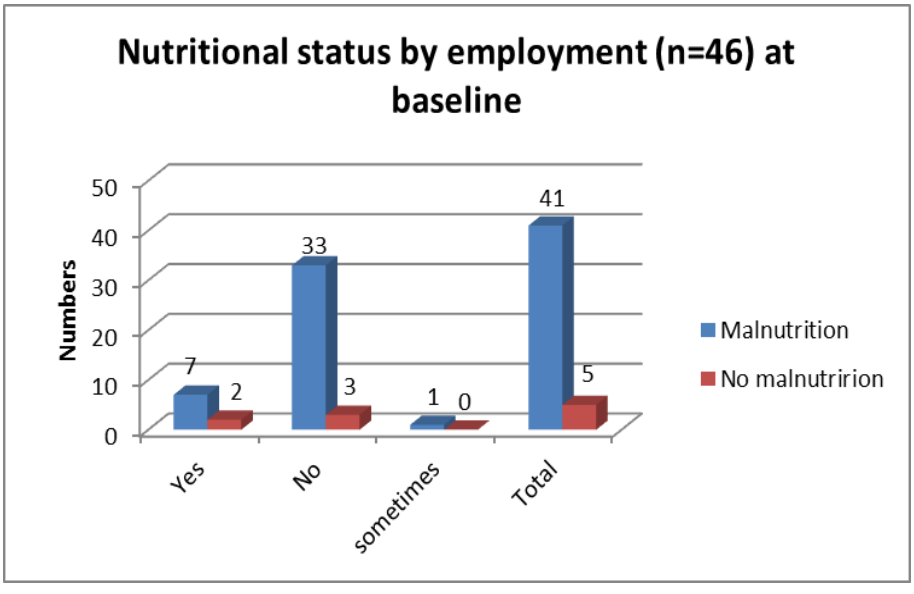


Figure 6

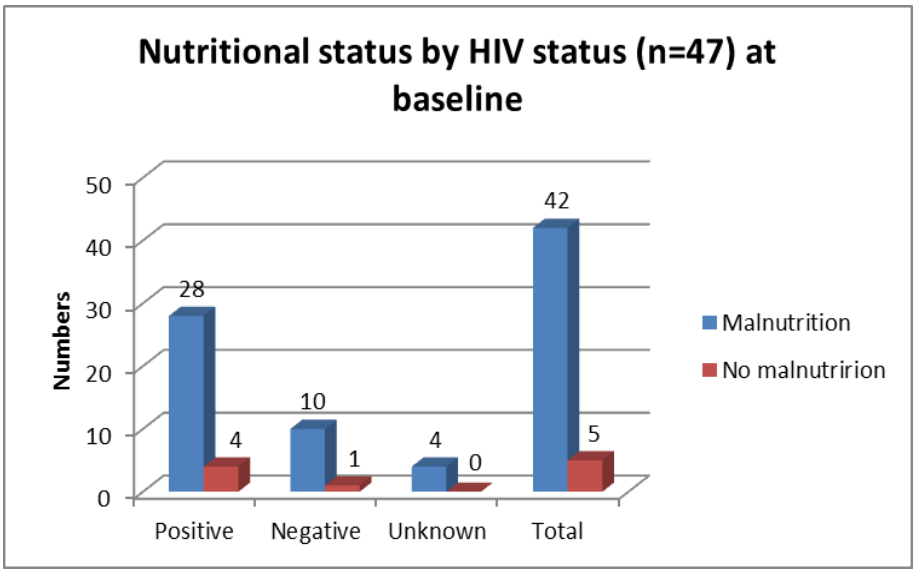


Figure 7

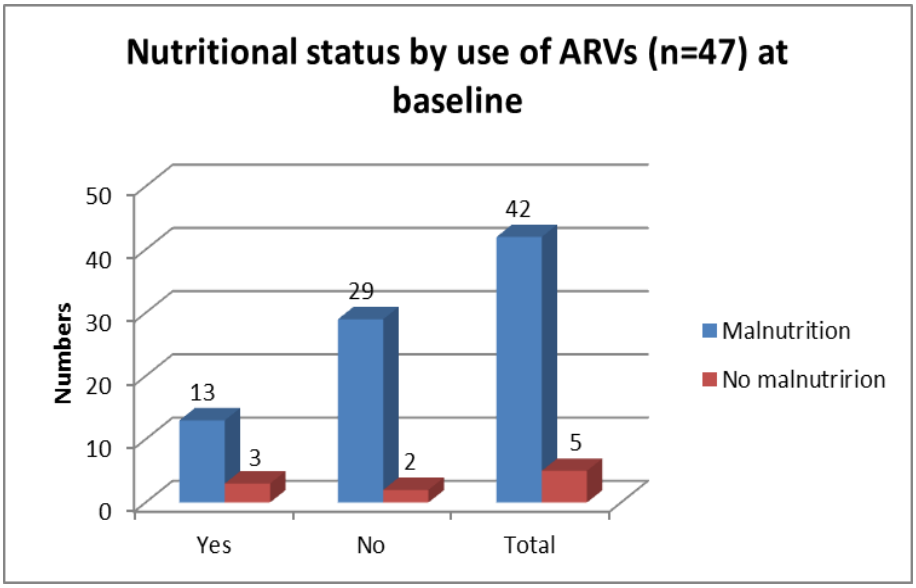
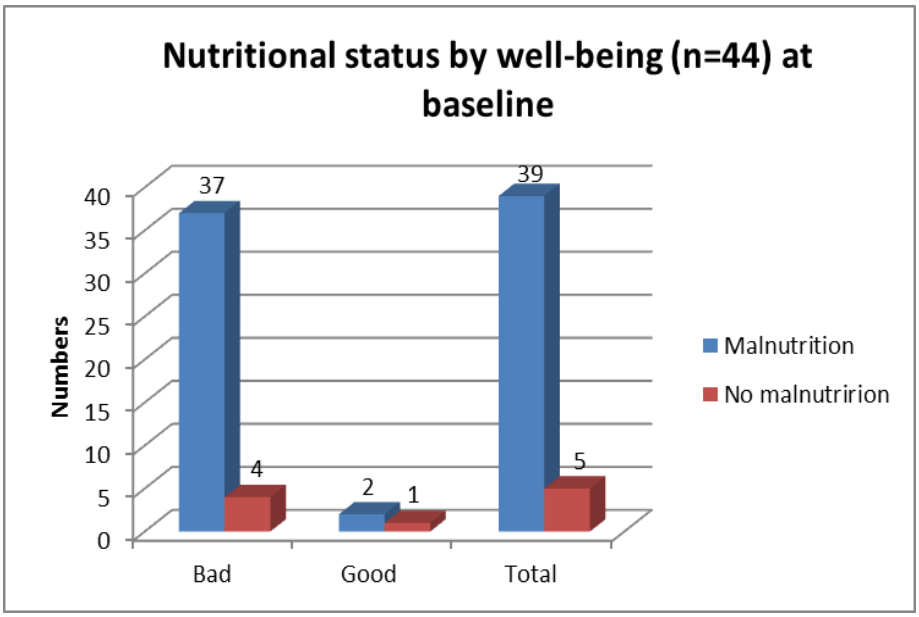
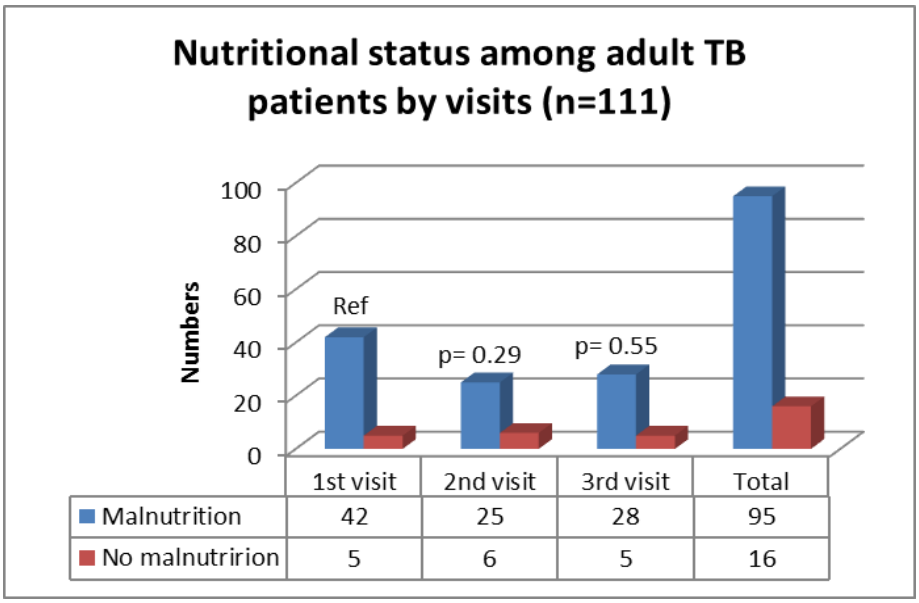


Figure 8



The following 3D bar chart (**Figure 9**) also shows the nutritional status among adult TB patients enrolled in 1st visit (baseline), 2nd visit and 3rd visit. There were no statistically significant difference for nutritional status of adult TB patients among visits (p=0.29 in 2nd visit and p=0.55 in 3rd visit).

Figure 9



The following **tables** (**4** and **5**) indicated both univariate analysis and multivariate analysis of the prevalence of OC among adult TB patients for 2 months follow-up.

For pseudomembranous candidiasis, univariate analysis showed an OR of 0.62 (95%CI 0.26 to 1.45) p>|z|= 0.27 for 2nd visit and OR= 0.06 (95%CI 0.01 to 0.46), p>|z|= 0.01 for 3rd visit respectively with 1st visit as a reference. Multivariate analysis showed an OR of 0.56 (95%CI 0.23 to 1.38) p>|z|= 0.21 for 2nd visit and OR = 0.05 (95%CI 0.01 to 0.38), p>|z| = 0.00 for 3rd visit respectively with 1st visit as a reference. There was statistically significance in 3rd visit for both univariate and multivariate analysis.

For erythematous, univariate analysis showed OR = 0.11 (95%CI 0.01 to 0.86) P>|Z|= 0.04 in 2nd visit and OR= 0.23 (95%CI 0.05 to 1.13) P>|Z|= 0.07 in 3rd visit respectively with reference to 1st visit. Multivariate analysis showed OR= 0.10 (95%CI 0.01 to 0.82) P>|Z|= 0.03 in 2nd visit and OR= 0.22 (95%CI 0.04 to 1.05) P>|Z|= 0.06 in 3rd visit respectively with a reference to 1st visit. This were statistically significant in 2nd visit for both univariate analysis (p= 0.04) and multivariate analysis (p=0.03).

For hyperplastic analysis, univariate analysis showed OR= 1.07 (95%CI 0.21 to 5.45) p>|z|= 0.94 in 2nd visit and OR= 0.76 (95%CI 0.12 to 4.70) P>|Z|= 0.77 in 3rd visit respectively with a reference to 1st visit. Multivariate analysis showed OR= 1.01 (95%CI 0.19 to 5.26) P>|Z|= 0.99 in 2nd visit and OR= 0.68 (95%CI 0.11 to 4.30) P>|Z|= 0.68 in 3rd visit. There was no statistically significance in 2nd and 3rd visit for both univariate and multivariate analysis.

The results for angular cheilitis were not displayed for 3rd visit due to the lack of subjects who showed angular cheilitis.

For Oral candidiasis (OC), univariate analysis showed OR= 0.45 (95%CI 0.22 to 0.95), P>|Z|= 0.04 for 2nd visit and OR= 0.15 (95%CI 0.06 to 0.43), P>|Z|= 0.00 for 3rd visit respectively with a reference to 1st visit. Multivariate analysis showed OR= 0.39 (95%CI 0.17 to 0.85), P>|Z|= 0.02 for 2nd visit and OR= 0.12 (95%CI 0.04 to 0.34), P>|Z|= 0.00 for 3rd visit. There was a statistically significant difference in the 2nd and 3rd visits for both univariate and multivariate

analysis. OC prevalence was found to be 5.7 times greater among TB-HIV co-infected patients compared to those TB patients who were HIV negative.

Table 4: Univariate analysis of Oral Candidiasis (OC) among adult TB patients after e'Pap intervention for 2 months follow-up

Variables	Total number (N) and percentage (%) of all Visits	Visits (1,2 and 3)					
		Visit-1	Visit-2	P>|Z|	Visit-3	P>|Z|	p value
Pseudo-membranous	**Yes** (N=27) (12%)	Ref	OR= 0.62 (95%CI- 0.26 to 1.45)	0.27	OR= 0.06 (95%CI- **0.01 to 0.46**)	**0.01**	**0.00**
	No (N=206) (88%)						
Erythematous	**Yes** (N=12) (5%)	Ref	OR= 0.11 (95%CI- **0.01 to 0.86**)	**0.04**	OR= 0.23 (95%CI- 0.05 to 1.13)	0.07	**0.01**
	No (N=221) (95%)						
Hyperplastic	**Yes** (N=8) (3%)	Ref	OR= 1.07 (95%CI- 0.21 to 5.45)	0.94	OR= 0.76 (95%CI- 0.12 to 4.69)	0.77	0.93
	No (N=225) (97%)						
Angular Cheilitis	**Yes** (N=9) (4%)	Ref	OR= 0.29 (95%CI- 0.06 to 1.42)	0.13	Empty	Empty	0.1
	No (N=224) (96%)						
Oral Candidiasis (Pseudo + Erythematous + Hyperplastic + Angular Cheilitis)	**Yes** (N=46) (20%)	Ref	OR= 0.45 (95%CI- **0.22 to 0.95**)	**0.04**	OR= 0.15 (95%CI- **0.06 to 0.43**)	**0.00**	**0.00**
	No (N=187) (80%)						

** Simple logistic regression model for different type of oral candidiasis **

Table 5: Multivariate analysis of Oral Candidiasis (OC) among adult TB patients after e'Pap intervention for 2 months follow-up with adjustment of HIV status

Factors	Pseudo-membranous (odd ratio, 95%CI and p value)	Erythematous (odd ratio, 95%CI and p value)	Hyperplastic (odd ratio, 95%CI and p value)	Angular Cheilitis (odd ratio, 95%CI and p value)	Oral Candidiasis (odd ratio, 95%CI and p value)
HIV status					
Negative	Ref (empty)	Ref	Ref (empty)	Ref (empty)	Ref
Positive	0.38 (0.14 to 1.02) 0.054	1.00 (0.19 to 5.16) 0.996	0.34 (0.07 to 1.52) 0.159	0.34 (0.74 to 1.52) 0.156	5.71 **(1.28 to 25.42) 0.022**
Unknown	(omitted)	2.44 (0.36 to 16.33) 0.359	(omitted)	(omitted)	17.41 (**3.42 to 88.69**) **0.001**
Visit					
Baseline(Visit-1)	Ref	Ref	Ref	Ref	Ref
Visit-2	0.56 (0.23 to 1.38) 0.211	0.10 (**0.01 to 0.82**) **0.032**	1.01 (0.19 to 5.26) 0.993	0.26 (0.05 to 1.32) 0.105	0.39 (**0.17 to 0.85**) **0.018**
Visit-3	0.05 (**0.01 to 0.38**) **0.004**	0.22 (0.04 to 1.05) 0.058	0.68 (0.11 to 4.30) 0.684	(empty)	0.12 **(0.04 to 0.34) 0.000**

** Multiple logistic regression model for different type of oral candidiasis **

The following 3D bar charts (**Figures 10**, **11**, **12**, **13** and **14**) display OC (Yes and No) and different kinds of OC among adult TB patients related to Visits (1, 2 and 3). Among them, pseudomembranous membranous candidiasis was statistically significance in 3rd visit (p=0.01). OC was also found to be statistically significant in both 2nd visit (p= 0.04) and 3rd visit (p= 0.00). The prevalence of OC was significantly decreased in both 2nd and 3rd visits with a reference to the 1st visit.

Figure 10

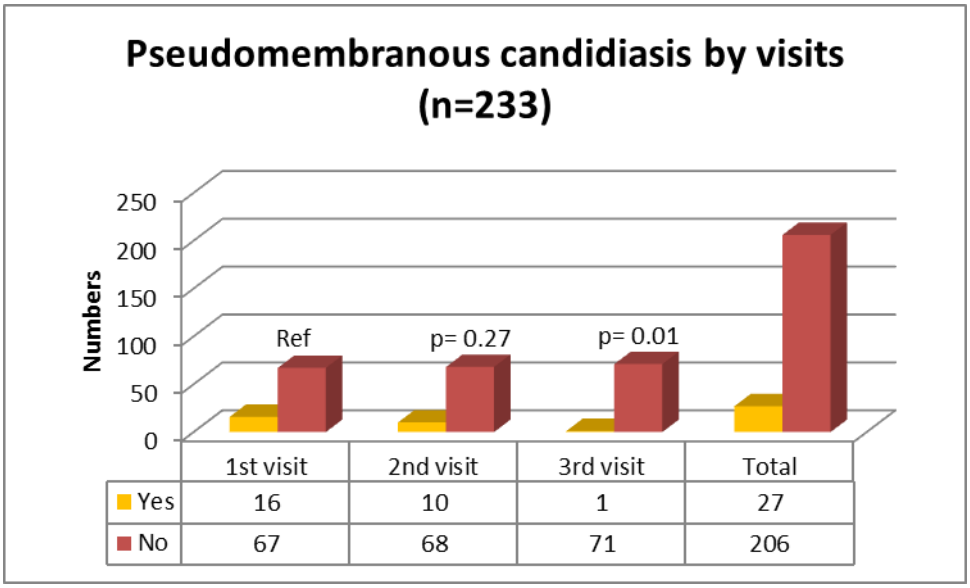


Figure 11

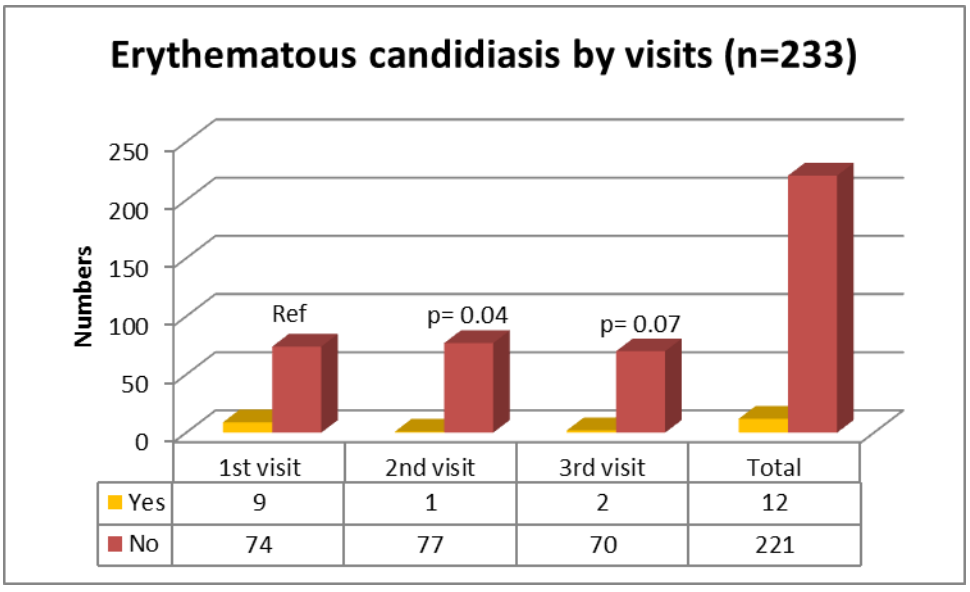


Figure 12

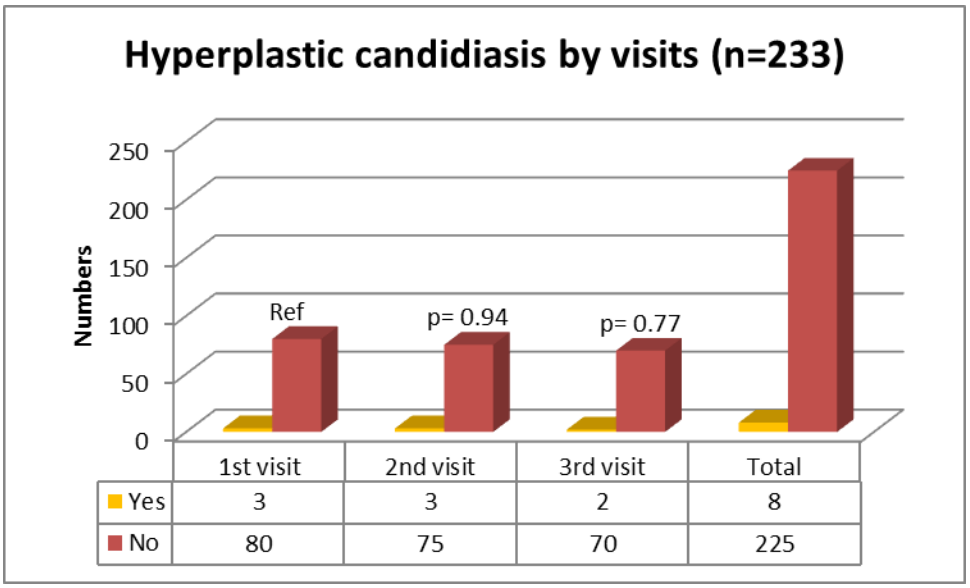
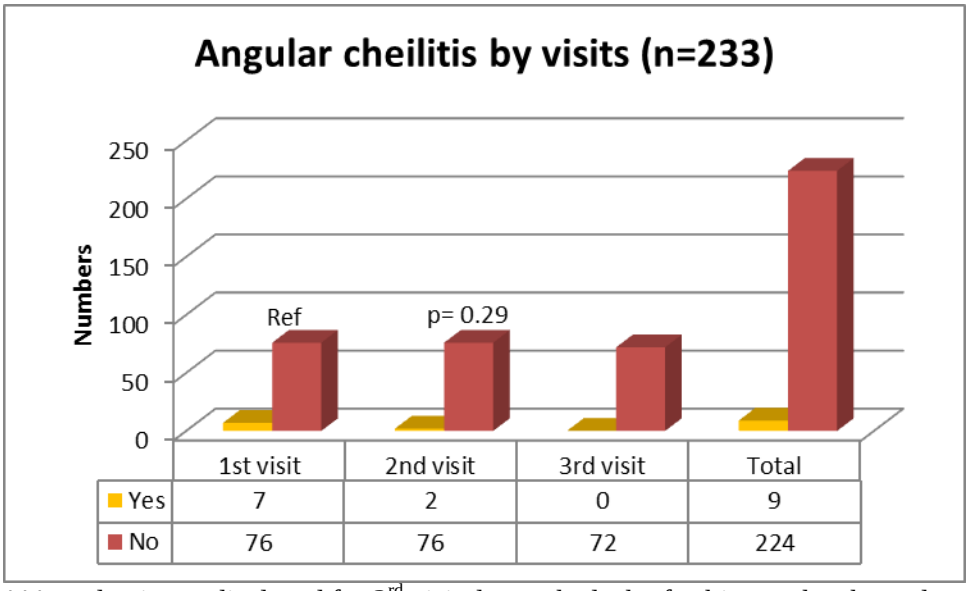
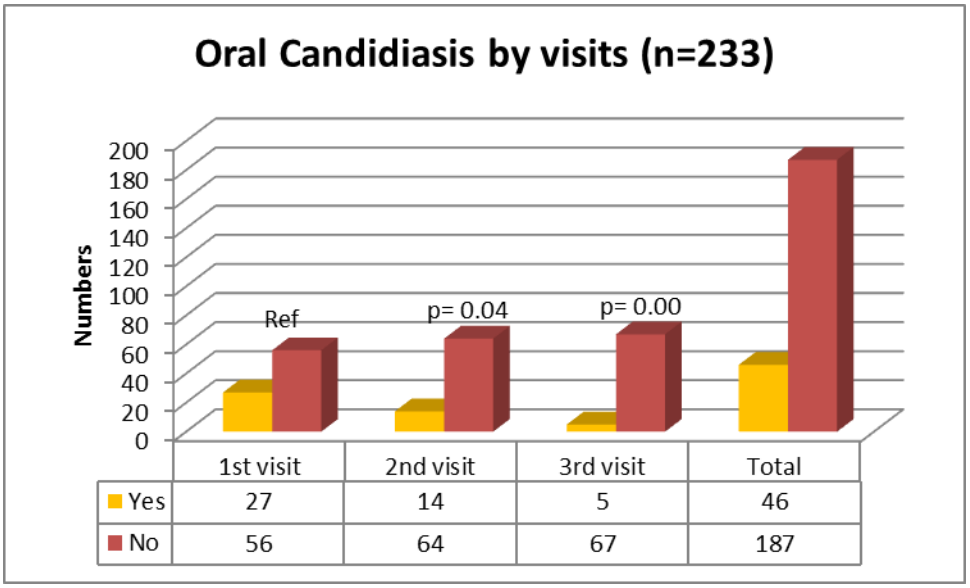


Figure 13



***p value is not displayed for 3rd visit due to the lack of subjects who showed angular cheilitis **

Figure 14


Oral Candidiasis by visits (n=233)
Numbers
200
180
160
140
120
100
80
60
40
20
0
Ref
p= 0.04
p= 0.00
1st visit
2nd visit
3rd visit
Total
Yes
27
14
5
46
No
56
64
67
187

CHAPTER 5: DISCUSSION

This study aimed to determine the effect of a fortified food, e'Pap, on oral candidiasis in adult TB patients attending clinic in Alexandra, Johannesburg, South-Africa in 2010.

5.1 Demographics, HIV and OC

The study revealed that 68% of TB patients were HIV+ while OC lesions among HIV-TB co-infected patients was 66% and only 7% OC among TB patients who were HIV negative. In the multivariate analysis, OC prevalence was found to be 5.7 times greater among TB-HIV co-infected patients compared to those TB patients who were HIV negative in multivariate analysis (OR 5.71, 95%CI 1.28 to 25.42, p = 0.022). This result was consistent with other previous studies except OC% among adult HIV patients was slightly different (54, 56, 60, 63, 64). HIV status (p= 0.00) was the only factor found to be statistically significant with micronutrient deficiency (those patients with poor wellbeing suffered the most from malnutrition). OC was found in nearly 37% of males and 63% among female patients (female predilection between TB/HIV and OC). But, prevalence of OC was not influenced by sex (p=0.62) and the results were also consistent with previous study done in Thailand (1997) to determine whether gender influences the occurrence of oral lesions [58] and also another study done in Nigeria (2006) about gender and oral manifestations of HIV infections among adults Nigerians [59]. A recent study done in Brazil (2013) showed that males had a significantly likelihood (four times higher than females) of presenting with this oral manifestation OR 4.3 (95% CI: 1.39-13.36) [60]. Therefore, it was difficult to make a conclusion and comparison of the current findings with other studies for the association between sex and OC. TB was found to be the most frequently occurring systemic co-infection in HIV infected people (most HIV patients have TB and most TB patients also have HIV in South Africa) [54,55]. Both HIV and TB have a synergistic interaction; each accentuates progression of the other and they are also consistent with the previous studies [32, 53, 55, 56].

5.2 Micronutrients and OC

Analysis of the data available for this study found no significant association between overall micronutrient level and the presence of OC at baseline. No studies also had been investigated for relationship between micronutrients (Selenium, Iron, Zinc, Vit-D and Vit-A) including albumin and OC but only one study was found investigated for relationships between nutritional factors (iron,

folic acid, vitamins, and carbohydrates) and pathogenesis of OC according to the current literature review. However there is little doubt that nutritional factors acting either locally or via systemic mechanisms could significantly affect the pathogenesis of oral candidiasis [61]. The results from the e'Pap intervention for adult TB patients in this South African study show that a short 2 months nutritional intervention can reduce the occurrence of OC (OR= 0.39, 95%CI 0.17 to 0.85, p= 0.02 for 2rd visit) and (OR= 0.12, 95%CI 0.04 to 0.34, p= 0.00 for 3rd visit).

5.3 Clinical sub-types of OC in relation to HIV/TB co-infection

A 1992 Greek cross sectional study which focused on oral signs and symptoms in 160 HIV-infected patients showed that the most common oral lesion in HIV/TB co-infected patients was candidiasis (61%).The authors also highlighted that OC is common and is sometimes an early manifestation of HIV infection [62]. This is in contrast to the approximately 32% prevalence seen in the 56 HIV/TB co-infected patients enrolled for baseline in the current South African study.

A study done in Thailand 1997 to assess the prevalence of oral lesions present in Thai people with AIDS and also to determine whether gender influences the occurrence of oral lesions. It was a cross-sectional study and oral examinations were performed on 124 AIDS patients (90 men, aged 19-62 years, median 30 years; and 34 women, aged 19-41 years, median 28 years). The study showed that 82% oral lesions were found in a group of Thai people with AIDS and pseudomembranous candidiasis was the most common lesion (54%) followed by erythematous candidiasis (25%), hairy leukoplakia (13%) and angular cheilitis (6%) respectively [58]. So, the results were similar to that obtained from the present study conducted in South Africa on e'Pap intervention in adult TB patients.

A study carried out in India in 2011 for oral manifestations of HIV infection and their correlation with CD4 count also showed that OC accounted for almost 40% (157 out of 306 oral lesions); erythematous candidiasis 30.6% (122 out of 306), pseudomembranous candidiasis 12.3% (49 out of 306), hairy leukoplakia 11.5% (46 out of 306) and angular cheilitis 4.3% (17 out of 306) [63]. OC was more commonly found in HIV-TB co-infected patients compared to those who are infected with only HIV. These results were also slightly different from the results of e'Pap intervention to

adult TB patients done in South Africa in which pseudomembranous candidiasis accounted for almost 46% (16 out of 35 OC) followed by erythematous candidiasis 25.7% (9 out of 35).

The study at the Khutsong and Heidelberg public health care facilities in Johannesburg, South Africa in 2005 showed that pseudomembranous candidiasis 80(38%), erythematous candidiasis 50(24%) and angular cheilitis 12(6%) among 210 patients ; all of whom were HIV positive [64]. These findings were comparable to the recent e'Pap intervention in South Africa in 2010 which also revealed that pseudomembranous candidiasis 16(45%), erythematous candidiasis 9(26%), hyperplastic candidiasis 3(9%) and angular cheilitis 7(20%) among adult TB patients (n=83); 67% of whom were HIV positive. This similarity was not unexpected in spite of the 5 years difference when the studies were done, the subjects came from a similar demographic area, both had a high prevalence of co-infection of HIV & TB and both samples had access ARV treatment.

A recent retrospective analysis of existing data collected from a large urban cohort of over 16,000 HIV infected adults who started ARV in Johannesburg, South Africa in 2011/12 indicated that there was a lower prevalence of OC (18%) compared to the OC (32%) found in the present e'Pap intervention among adult TB patients. The lower prevalence of OC in the urban cohort study could be explained by the huge difference in sample size, no standardized clinical assessment of OC and perhaps a greater adherence to the ARV treatment.

For different clinical types of OC among HIV patients, the overall results from e'Pap intervention to adult TB patients in South Africa were generally consistent with other studies in Greece (1992) and Thailand (1997) except for a recent study done in India (2011) which showed a male predominance in OC and erythematous candidiasis was most common lesion.

5.4 Limitations

A small numbers of adult TB patients (83) enrolled in 1st visit (baseline) and a few subjects loss to follow-up (2nd and 3rd visits) are the biggest limitations of this study. Reporting bias may have been introduced from the primary study as participants may have provided unreliable information concerning their socio-economic status, food insecurity and social support to the investigators. Some participants declined to continue with the study (resulting in loss of follow up from a primary

study which may introduced bias and reduced the reliability and validity of the results). Ethical considerations (most likely conflict of interest in participants) may limit participation in the study and/or withholding others from the intervention.

CONCLUSIONS

Regarding OC and micronutrient intervention for TB patients, previous studies focused on the general health of people concerning to nutrition/micronutrients (5,6,7,15,16,24,25,31,33,42) and few on oral health, HIV and HIV-TB co-infected patients (56,57,58,59, 64, 65). No studies have focused on different kinds of clinical OC related to micronutrients intervention among adult TB patient according to current literature review. This study is the first one to investigate an association between different kinds of common OC and micronutrient intervention. 59% (16 out of 27 OC) among adult TB patients were pseudomembranous candidiasis. Relative low levels of micronutrients such as Vit-A 62% (28 out of 45), Zinc 34% (14 out of 41), Iron 55% (26 out of 47) and Selenium 8% (3 out of 37), including Albumin 42% (20 out of 47) were found in baseline but no statistically significant differences was found for each of the micronutrients related to OC (p=1.00). However, there was a statistically significant improvement in overall clinical different types of OC (Oral Candidiasis) among adult TB patients for both 2nd and 3rd visits using univariate analysis p=0.04 (95%CI 0.22 to 0.97) and p=0.00 (95%CI 0.06 to 0.43) and also multivariate analysis p=0.01(95%CI 0.17 to 0.85) and p=0.00 (95%CI 0.04 to 0.34). In spite of the relatively short period of micronutrient intervention, this analysis shows the potential beneficial effect of e'Pap for adult TB patients and it could be of great benefit in addressing OC in adult TB patients.

Recommendation

The following recommendations are suggested.

- The number of subjects for this study should be increased and recruited from a wider range of settings.
- A control group (no micronutrient supplementation group) should be included in any future study to improve sensitivity and reliability of analysis results.
- The study duration should be extended for a longer follow-up period.
- Nutritional supplementation with e'Pap should be encouraged among adult TB patients.
- More attention should be given to addressing poverty, wellbeing and employment status.

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Appendix A: Personal Record Sheet

Reference #	
Gender	
Date of Birth	
Household Employment Status: (Does anyone in your household work?)	1=yes; 2=no; 3=sometimes; 4=don't know
How many people stay at your home? (include adults, children and infants)	

TB records (participants only)

Category First Treatment Relapse Re-treatment after Failure Re-treatment after Default			
Treatment Start Date			
Treatment Regimen			
Treatment Change?			
Weight at Diagnosis (kilograms - to the nearest decimal)			
Outcome • Cured • Treatment Completed • Treatment Defaulted • Treatment Failure • Died			
	Pre-treatment	End of Intensive	End of Treatment
Date			
Sputum Result			

Appendix B: Medical History

Ref #	
Date of Attendance (ddmmyy)	
Wellbeing (On a scale of 1 = very bad 2 = bad; 3 = ok; 4 = good; 5 = very good)	
Appetite (0 = Poor, 1 = Good)	
Change in eating habits (0 = no change, 1 = less, 2 = more, 3 = different)	
Supplement regularly consumed? (0 = no; 1 = yes)	
Alcohol (0 = none; 1 = once a week; 2 = every day; 3 = - undisclosed)	
Dagga (0 = none; 1 = once a week; 2 = every day; 3 = undisclosed)	
Tobacco (0 = none; 1 = once a week; 2 = every day; 3 = undisclosed)	
Vomiting (0=no, 1=yes)	
Fever (0=no, 1=yes)	
Sores on skin (not healing for more than 1 week)	
Coughing often (0=no, 1=yes)	
Continuous runny nose (0=no, 1=yes)	
Diarrhoea often (0=no, 1=yes)	
Constipation (0=no, 1=yes)	
Night sweats (0=no, 1=yes)	

Low energy / feeling tired all the time (0=no, 1=yes)	
Bloating (0=none; 1=occasionally; 2=often)	
Oedema (esp. swollen ankles)(0=no, 1=yes)	
Height (in cm)	
Weight (in kg)	
Waist circumference (in mm)	
Hip circumference (in mm)	
MUAC (in mm)	
Skinfold – Triceps (Back of Upper Arm) (in mm)	
Skinfold – Subscapular (Under Shoulder Blade) (in mm)	
Skinfold – Supra-Iliac (Hip) (in mm)	

Appendix C: Adult Oral Health Status (Data Capture Sheet)

1. Refer no.……..

2. Week ……

3. Extra-Oral Examination

HIV/AIDS oral manifestations (Including 4 majors types of Oral Candidiasis)

CONDITION	LOCATION
1 No abnormal condition	17 upper lip
2 Pseudomembranous Candidiasis	18 lower lip
3 Erythematous Candidiasis	19 mucosa of the upper lip
4 Hyperplastic Candidiasis	20 mucosa of the lower lip
5 Angular Cheilitis	21 mucosa around the corner on R side
6 Herpetic Ulceration	22 mucosa around the corner on L side
7 Apthous Ulceration	23 cheek mucosa on R side of patient
8 Infective (TB, STDs) Ulceration	24 cheek mucosa on L side of patient
9 Atypical Ulceration	25 mucosa of upper jaw, bet lip/cheek & gums
10 Erythema Multiformae	26 mucosa of lower jaw, bet lip/cheek & gums
11 Oral Hairy Leukoplakia	27 mucosa of gums of upper teeth
12 Kaposi's Sarcoma	28 mucosa of gums of lower teeth
13 Non-Hodgkin's lymphoma	28 top surface of tongue
14 HPV - related lesions	29 sides of tongue
15 Leukoplakia	30 under surface of tongue
16 Melanotic hyperpigmentation	31 mucosa bet undersurface of tongue & gums of L teeth
	32 mucosa of hard palate
	33 mucosa of soft palate
	34 mucosa behind last molar of U & L jaws

CONDITION	LOCATION

Other

……

……

Appendix D: Participant Information Sheet

Hello, Good day

My name is……..I am …….I would like to invite you to participate in a study I'm conducting entitled

"……;".

What is the purpose of the Study?

……

……

What the study entails?

The research process includes the following.

- Questions about your personal details (i.e. age, gender and household income status).
- Questions relating to your HIV and TB status – this will be done privately, in full confidentiality.
- Measurement of your height, weight, body mass index calculation and waist circumference.
- Examination of the mouth will be done using a mirror, probe and light.
- Blood sample of 10ml will be collected from each participant to measure nutrients levels.
- Blood will be discarded after nutrient analysis and the findings will be kept confidential.
- The collection of blood samples may involve mild discomfort or pain.
- The blood sample and health status information will be kept confidential as every participant will be allocated a reference number.
- The full examination will take about 15 minutes.

If there are any questions you do not wish to answer, you are free not to answer these questions.

Risks

……

……

……

Benefits

……
……
…….

Confidentiality:

All information obtained from you will remain confidential. Only the researcher will have access to the data. The information collected will be kept in a secure and locked office.

Participation is voluntary:

Participation is voluntary and you are free not to participate or to respond to any questions. Refusal to participate or discontinue will not disadvantage you in any way or you're your treatment.

Further information:

If you enquire any further information or have any questions/complaints on the study, pls contact,……
……..

You may also contact Anisa Keshav at Wits on 011 274 71234 for questions around study ethics of the University of Witwatersrand Human Ethics Committee.
Your consideration to participate in the study is greatly appreciated. If you are happy to take part in the study, please read and sign the attached consent form.

Thank you,

Your name and title

……..
……..
……..

Appendix E: Consent Form:

Date: ……

I have read the information sheet about the study and had it explained to me. I understood the purpose of the study.

I also understand that I have the right to cease participation at any time and to refuse answering certain questions. I am told that there will be no risks for mw to take part or not to take part in the study.

I understand that my confidentiality will be carefully guarded and no one outside the research team will be able to know about my answers, health and oral status. I understand that a reference number will be allocated to me to maintain anonymity.

Signature of respondent (If yes)…….

Initials of investigator…….

Contact details of main researcher:

……

……

……

……

Appendix F: e'Pap Composition

Table 1. e'Pap Composition.

	Unit	Per 100 gm	Adult RDA	% of Adult RDA per 100 gm
Energy	KJ	1556		
Protein	gm	12.7		
Carbohydrate	gm	63.6		
Total Cereal Fat	gm	7		
Total Dietary Fibre	gm	10		
Potassium	%	0.46		
Sodium	%	0.5		
Vitamin A	RE	1000	1000	100
Vitamin B1	mg	1.4	1.4	100
Vitamin B2	mg	1.6	1.6	100
Vitamin B3	mg	18	18	100
Vitamin B5	mg	6	6	100
Vitamin B6	mg	2	2	100
Vitamin B12	µg	1	1	100
Vitamin C	mg	60	60	100
Vitamin D3	µg	5	5	100
Vitamin E	mg	10	10	100
Folic Acid	µg	200	200	100
Biotin	µg	100	100	100
Iron	mg	14	14	100
Zinc	mg	15	15	100
Iodine	µg	150	150	100
Calcium	mg	220	800	28
Magnesium	mg	45	300	15
Manganese	mg	0.45		
Copper	mg	0.3		
Selenium	µg	200		
Vanadium	µg	50		
Chromium	µg	30		
Molybdenum	µg	30		

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Appendix G: Ethical Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Mr UWL Phyo

CLEARANCE CERTIFICATE	**M120723**
PROJECT	The Effect of a Fortified Food, e'Pap on Oral Candidiasis in Adult TB Patients over a Three Month Follow-Up Period
INVESTIGATORS	Mr UWL Phyo.
DEPARTMENT	School of Public Health
DATE CONSIDERED	27/07/2012
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 27/07/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof M Rudolph

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...