academicJournals

Vol. 7(21), pp. 2430-2437, 21 May, 2013
DOI: 10.5897/AJMR2013.5594
ISSN 1996-0808 ©2013 Academic Journals
http://www.academicjournals.org/AJMR

African Journal of Microbiology Research

Review

A South African perspective on *Helicobacter pylori*: Prevalence, epidemiology and antimicrobial chemotherapy

Nicoline F. Tanih[1] and Roland N. Ndip[1, 2]*

[1]Microbial Pathogenicity and Molecular Epidemiology Research Group, Department of Biochemistry and Microbiology, Faculty of Science and Agriculture, University of Fort Hare, P/Bag X1314, Alice 5700, South Africa.
[2]Department of Microbiology and Parasitology, Faculty of Science, University of Buea, P O Box 63, Buea, Cameroon.

Accepted 10 May, 2013

The spiral shaped Gram-negative bacterium, *Helicobacter pylori* colonizes the stomach of more than 50% of the world's population and can persist for a lifetime if not completely eradicated. High prevalence of the bacterium is common in most population although a majority of the infected patients remain asymptomatic; with only a small subset of infected people experiencing *H. pylori*-associated illnesses such as chronic gastritis, gastric and duodenal ulcers, mucosa associated lymphoid tissue lymphoma as well as adenocarcinoma. *H. pylori* is common in South Africa with prevalence ranging from 50 - 84% as depicted in the various studies conducted across the country. Infection is usually acquired in childhood and is associated with low socio-economic status, overcrowding, poor sanitation and unclean water supplies which appear to influence the rate of transmission. Eradication of this pathogen is a global challenge due to its alarming rate of drug resistance. Triple therapy consisting of a proton pump inhibitor and clarithromycin and either metronidazole or amoxicillin, is recommended for treatment. In this article, we review the major studies conducted based on *H. pylori* prevalence, epidemiology and antimicrobial chemotherapy in South Africa. Overall, the results of the findings indicate a high prevalence of *H. pylori*, resistance to recommended therapy and identified the need to consider natural products, including medicinal plants and honey as leads, which may offer useful alternatives in the treatment of *H. pylori*-related infections in South Africa and the world at large.

Key words: *Helicobacter pylori*, prevalence, epidemiology, chemotherapy, South Africa.

INTRODUCTION

The human gastric pathogen, *Helicobacter pylori* (*H. pylori*) infect more than half a million of the world's population. It is a spiral, Gram-negative, microaerophilic, motile, curved rod that inhabits the gastric mucosa of the stomach (Ahmed et al., 2007; Tanih et al., 2009). Since its discovery, *H. pylori* has been related to a number of gastro-duodenal pathologies such as chronic gastritis, peptic ulcer, duodenal ulcer, non-ulcer dyspepsia, mucosal associated gastric cancers and gastric mucosa-associated lymphoid tissue (MALT) lymphoma (Ahmed et al., 2007; Ndip et al., 2008). However, only a subset of infected persons actually present with *H. pylori* associated illness (Tanih et al., 2009). Enlightenment of the involvement of *H. pylori* in the pathophysiology and treatment of peptic ulcer disease was one of the most important developments in medicine in the 20th Century. Its association with gastric cancer warranted it's classification as a class-1 carcinogen by the World Health Organization (Delport et al., 2006; Tanih et al., 2009).

Tremendous diversity is known to exist amongst strains

*Corresponding author. Email: rndip@ufh.ac.za or ndip3@yahoo.com. Tel: (+27) 782 69619. Fax: (+27) 866 22 4759.

of *H. pylori* which varies geographically and even between ethnic groups, and races in the same region (Wirth et al., 2004). Carriage of *H. pylori* is usually long term and begins most often in infancy (Kidd et al., 1999a; Segal et al., 2001; Tkachenko et al., 2007). Frequently, the infection starts in the antrum and spreads to the corpus after extensive mucosal damage. A high prevalence of *H. pylori* has been reported in Africa presenting as the main cause of at least 90% of duodenal ulcers and 70% of gastric ulcers on the continent (Louw et al., 1993; Ndip et al., 2004; 2008; Tanih et al., 2010a). In various regions of sub- Saharan Africa, the pathogen has been isolated in about 61- 90% of per-sons (Holcombe, 1992; Kidd et al., 1999a). Involvement of *H. pylori* in gastric patients in Cameroon (Ndip et al., 2008) revealed a similar pattern to that recorded among Ghanian patients (Baako et al., 1996) with dyspeptic symptoms and in South African patients with non-ulcer dyspepsia (Louw et al., 1993). Interestingly, prevalence does not parallel the incidence of morbidity caused by the infection. For example, in Africa, the prevalence of infection is very high but the incidence of gastric carcinoma and other *H. pylori*-associated morbidities is relatively low. This apparent anomality has been termed the 'African enigma' (Holcombe, 1992; Kidd et al., 1999a; Ahmed et al., 2007).

H. pylori infection is common in South Africa, as might be expected in developing countries (Pelser et al., 1997; Mosane et al., 2004). Reports on prevalence of the organism in the country are mostly derived from seroprevalence data (Kidd et al., 1999a; O'keefe et al., 2000), which does not provide more information other than the presence of antibodies, which are poor mar-kers of active infection. However, some investigators have used alternative phenotypic (such as culture) or molecular based methods to report on the prevalence of the organism in their study area in the country (Kidd et al., 1999b; Louw et al., 2001; Kidd et al., 2001; Tanih et al., 2010a; 2010b). For example, we reported an overall prevalence of 66.1% (168/254) using culture based methods and amplification of some conserved genes in our study in the Eastern Cape Province, revealing a generally high prevalence in the province (Tanih et al., 2010a).

Man is still the known reservoir to *H. pylori*. Domestic animals have also been reported as potential reservoirs in the spread of infection but their role still remains unclear (Fox et al., 1995). However, spread of the organism has also been known to be associated to water or uncooked vegetables contaminated with sewage and a host of other factors (Dube et al., 2009a). The putative routes of transmission of the organism have been reported to be faecal-oral, oral-oral, and gastric-oral (Brown, 2000).

Conventionally, reliable treatment of *H. pylori* infection requires two or more antibiotics coupled with a proton pump inhibitor. Despite this range of antibiotics, the problem of drug resistance to most of them is well established (Ndip et al., 2008; Tanih et al., 2009; Tanih et al., 2010c) and presents a major concern. Primary resistance against clarithromycin and metronidazole is common in many countries, while resistance to different antibiotics used as first-line treatment varies between countries and communities, and may change with time and geographical location (Tanih et al., 2010c). However, resistance has been reported to most of these antibiotics and occasionally, with side-effects such as nausea, vomiting, epigastric pain, abdominal discomfort and/or diarrhoea (Kawakami et al., 2006). Eradication of this organism leads to improvement of gastritis and tremendously decrease relapse of gastric and duodenal ulcers. Hence, there is the need to seek for complementary and alternative treatment to circumvent the associated problems.

Natural products, including medicinal plants and honey, may offer useful alternatives in the treatment of *H. pylori*-related infections. We have studied different plants and honey for their activity against *H. pylori* (Okeleye et al., 2010; 2011; Manyi-Loh et al., 2010; Njume et al., 2011a). Njume et al. (2011a) investigated a number of plants including *Combretum molle*, *Sclerocarya birrea*, *Garcinia kola*, *Alepidea amatymbica* and some *Strychnos* species for their anti-*H. pylori* activity. Also, Okeleye et al. (2010; 2011) in their studies demonstrated the anti-*H. pylori* activity of *Bridelia micrantha* and *Peltophorum africanum*, respectively.

The antimicrobial activity of honey is now well documented (George and Cutting, 2007; Ndip et al., 2007a; Manyi-Loh et al., 2010). Manyi-Loh and co-workers investigated the anti-*H. pylori* activity of three South African honeys; Pure honey, citrus blossom and goldcrest and found that all honey varieties demonstrated varying levels of anti-*H.pylori* activity (Manyi-Loh et al., 2010).

In this communication, we provide information emanating from our laboratory and other groups in South Africa on the prevalence, epidemiology and antimicrobial chemotherapy of *H. pylori* in an effort to continuously highlight the clinical and epidemiological significance of this notorious pathogen in our environment.

PREVALENCE OF HELICOBACTER PYLORI

Infection with *H. pylori* is associated with substantial morbidity and mortality with a high prevalence reported worldwide. Studies conducted in different parts of the world have revealed the presence of this organism in their study population (Holcombe, 1992; Baako et al., 1996; Ndip et al., 2008; Tanih et al., 2010a). The prevalence of infection seems mostly to depend on the rate of acquisition, rate of loss of infection and the length of the persistence period between acquisition and loss (Segal et al., 2001). As such, prevalence varies with geographical region and even between ethnic groups of the same region (Louw et al., 1993; Segal et al., 2001; Tanih et al., 2010a). Wide variation in prevalence exists between the more affluent urban populations and the resource-poor rural

populations. The highest rates of *H. pylori* prevalence have been reported in Eastern Europe, Asia, and many developing countries and developing populations in developed countries (for example, Native Americans) (Tkachenko et al., 2007).

The variations seen in the prevalence of infection between and among populations may point to the fact that parameters such as age, cultural background, genetic predisposition, socio-economic status and environmental factors all play a role in the acquisition and transmission of *H. pylori* (Segal et al., 2001; Dube et al., 2009b). Attracting attention is the high prevalence of *H. pylori* infection in developing countries which does not commensurate the low prevalence of gastric cancer unlike in developed nations with a generally low prevalence of infection and yet a high prevalence of gastric cancer (Holcombe, 1992). Typically, infection with *H. pylori* is acquired early in childhood but it is difficult to ascertain when infection occurs clinically hence seroprevalence data are the source of information of *H. pylori* rates both in geographically and demographically diverse populations (Kidd et al., 1999a; Logan and Walker, 2002). A high prevalence of this organism has also been reported in children in the Western World (Thomas et al., 2004).

Africa is home to *H. pylori* infection as very high prevalence rates have been reported in different studies conducted on the continent, revealing the presence of the organism in 61-100% of the study populations (Holcombe, 1992; Segal et al., 2001; Ndip et al., 2004; 2008; Tanih et al., 2010a); the organism has been associated with at least 90% of duodenal and 70% of gastric ulcers (Ndip et al., 2008; Tanih et al., 2010a). Infection with the organism is common in South Africa as is also the case in most developing countries (Segal et al., 2001; Tanih et al., 2010a). Childhood acquisition is common with more than 50% of all children in South Africa being infected by the age of 10 years, with prevalence rising to 80% in adults (Kidd et al., 1999a). Pelsar et al. (1997) documented a high prevalence (67 - 84%) of *H. pylori* antibodies in children in Bloemfontein, while Mosane et al. (2004) also reported *H. pylori* IgG antibodies in South African mothers and their children. In another study, Samie et al. (2007) described a prevalence of 50.6% among children <5 years old in their study in Thohoyandou, North of South Africa. Fritz et al. (2006) used the *ureB* and *glmM* genes to delineate the incidence of *Helicobacter felis* and the effect of coinfection with *H. pylori* in a prevalence study in South Africa, reporting a high prevalence of the organism [83.3% (*ureB*) and 78.9% (*glmM*)] linked to these genes. Tanih et al. (2010a) examined *H. pylori* infection in patients with gastric-related morbidities in the Eastern Cape Province of South Africa, reporting an overall prevalence of 66.1% (168/254). In another study of asymptomatic individuals aged 3 months to ≥ 60 years in the Eastern Cape Province, we observed *H. pylori* antigenemia in 86.8% of stools of our study subjects (Dube et al., 2009b) using a sandwich-type enzyme immunoassay amplification technology (Amplified IDEIA Hp StAR, Oxoid, UK) which detects *H. pylori* antigens using monoclonal antibodies specific for *H. pylori* antigens.

Prevalence increased with age from 75.9% in children < 12 years age to 100% in young adults aged 25-47 years and subjects aged ≥ 60 years ($P < 0.05$) (Dube et al., 2009b). We concluded that there was a high prevalence of *H. pylori* antigens in fecal samples of asymptomatic individuals in the Nkonkobe municipality, an indication of active infection. Kidd et al. (2001) also reported the presence of the organism in most dyspeptic subjects employing endoscopic approach. Louw et al. (2001) in their study in Cape Town documented an *H. pylori* prevalence that ranged from 60% using the rapid urease test to 79% with serology. A low prevalence (approximately 3%) of *H. pylori* was reported in specimens obtained from the oral cavity in a study by Goosen et al. (2002) in Pretoria.

Studies correlating the prevalence of the organism and disease status have been conducted. In Cape Town, Louw et al. (1993) documented an overall incidence of *H. pylori* infection in 63% of their patients with non-ulcer dyspepsia (NUD), 80% of gastric ulcer (GU) and 95% of duodenal ulcer (DU) based on histology reports; while O'Keefe et al. (2000) reported prevalence rates of 78%, 81%, and 81% in patients with gastric cancer (GC), peptic ulcer (PU) and NUD, respectively based on serology testing. In a similar study in the Eastern Cape Province, we reported the highest *H. pylori* prevalence in patients with NUD (32.7%; 55/168), and lowest (0%; 0/168) in those with atypical oesophageal reflux disease and gastroduodenitis (Tanih et al., 2010a).

Other studies on prevalence have focused on virulence genes such as *vacA*, *cagA*, *iceA* etc, in different studies across the country (Ally et al., 1999; Kidd et al., 1999b; Kidd et al., 2001; Tanih et al. 2010b). In the Eastern Cape Province, we reported a very high prevalence of *vacA*, *cagA* and *IceA* in our study population (Tanih et al., 2010b). *CagA*, for example, was identified in 90% of the strains investigated affirming the statement "South African *Helicobacter pylori* isolates are characterised by the universal presence of *cagA* but have differences in vacuolating cytotoxin gene (*vacA*) alleles which correlate with clinically significant disease" (Kidd et al., 2001). Astoundingly, a high prevalence of *iceA* genotype has also been reported in South African clinical isolates (Kidd et al., 2001; Tanih et al., 2010b).

South Africa has a heterogeneous population including white, black and coloured. In our study in the Eastern Cape Province relating race and disease status, we observed the highest infection rate in coloureds (68.4%; 89/130) and lowest in whites (59.5%; 25/42) (Tanih et al., 2010a). However, there was no statistically significant difference ($P>0.05$) between the races, contrary to Louw et al. (1993) who observed a marked difference in prevalence amongst ethnic groups, 40% in whites and 71% in coloureds ($P < 0.001$). The variation in acquisition of

infection among ethnic and racial groups appears to be primarily related to differential exposure (Segal et al., 2001). The generally high prevalence of human infection seen in South Africa and the world at large are an indication that effective public-health interventions need to be developed.

EPIDEMIOLOGY

Human infection with *H. pylori* has a worldwide distribution (Dube et al., 2009a; Tanih et al., 2009). Investigation on the incidence of the organism has been difficult because acute infection does not present with diagnostic symptoms, hence it is impossible to pinpoint the time a person acquires the infection (Kidd et al., 1999a; Logan and Walker, 2002). The associated cost and unreliability of the testing methods (non-invasively) in young children have all hampered on this. However, incidence of the infection can be determined by extrapolation from the prevalence data. Transmission pathways for medically important bacteria are important to our understanding of pathogens (Delport et al., 2006). The spread and acquisition of *H. pylori* has been generally linked to a number of factors including density/crowding, social factors and family history of gastric disease, smoking, alcohol consumption, occupational exposure, waterborne exposures, hygienic practices, deficiency of proper sensitization and poor diet (Brown, 2000; Ndip et al., 2004; Dube et al., 2009a; 2009b).

Other than the human stomach, there are other 'vessels' that are known reservoirs for *H. pylori*. Animals, for example, cats, and monkeys among others harbour organisms that resemble *H. pylori* but under particular circumstances (Tanih et al., 2009). These animals could be reservoirs for human infection. Neither a zoonotic reservoir nor food appears to be significantly involved in acquisition of *H. pylori*. Thus the major question of transmission remains on how *H. pylori* move from the stomach of one person to that of another. Several studies on epidemiology have tried to trace transmission trend and possible reservoirs of this organism. However, knowledge of reservoirs and transmission modes remain poor (Thomas et al., 2004; Ndip et al., 2004). Factors such as host and bacterial genetic as well as the environment have been used to trace the causative link of *H. pylori* infection (Delport et al., 2006). However, some possible routes for transmission of *H. pylori* have been suggested.

The faecal-oral route appears to be the most important route of transmission (Tanih et al., 2009). Delport et al. (2006) conducted a study in South Africa to infer transmission of the organism and demonstrated that transmission had a strong nonfamilial component. A study conducted by Dube et al. (2009a) in the Eastern Cape Province of South Africa revealed a high prevalence (86.8%) of the organism in faecal samples of healthy individuals. Based on this, faecally contaminated water and food were indicated as a likely source of infection of the organism in the country though isolation of the organism from water proves difficult (Dube et al., 2009a). Food-borne transmission and unclean hands have also been substantiated however; this is yet to be elucidated in South Africa. The oral cavity was evaluated as a reservoir from where *H. pylori* may be transmitted however; the organism was not detected in dental samples (Olivier et al., 2006). On the contrary, prevalence as low as approximately 3% was reported in specimens obtained from the oral cavity in another study in Pretoria (Goosen et al., 2002). Although a number of studies have demonstrated the role of gastro-oral, iatrogenic, sexual transmissions, horizontal transfer and intrafamilial clustering (Brown, 2000; Eslick, 2000; 2002; Delport et al., 2006; Fritz et al., 2006; Kast, 2007) in the transmission of *H. pylori*; no studies have been done in South Africa to ascertain the role of these routes in the transmission of the organism.

ANTIMICROBIAL CHEMOTHERAPY

The tenacity of *H. pylori* infection and the associated morbidity and mortality make effective treatment regimens extremely important. Unfortunately, infection with this organism presents a unique therapeutic challenge (Tanih et al., 2010c). Determination of the most favourable treatment is difficult because the organism lives in an environment not easily accessible to many medications. However, eradication of *H. pylori* is the first therapeutic approach and constitutes acceleration of ulcer healing and reduction of the rate of ulcer complications and a reliable long-term prophylaxis of peptic ulcer relapse (NIH, 1994).

Optimal treatment of *H. pylori* require the application of triple therapy which is generally recommended for eradication and conventionally consists of a proton pump inhibitor, clarithromycin and either metronidazole or amoxicillin (Louw et al., 1998; Kalach et al., 2001, Tanih et al., 2010c). In previous studies, Louw et al. (1992) demonstrated that overall eradication rates did not differ between South African patients treated with the use of sucralfate and bismuth compound in triple therapy. Also, the use of bismuth compounds which protect the stomach lining has enhanced the efficacy of triple therapy.

Most strains of *H. pylori* are susceptible *in vitro* to commonly used antibiotics such as; amoxicillin, tetracycline, metronidazole and clarithromycin (Nash et al., 2003; Tanih et al., 2010c). There are however regional differences in success rates that are not completely explained by resistance to either metronidazole or amoxicillin. For second-line therapy, quadruple therapy using a proton pump inhibitor with bismuth, metronidazole and tetracycline (proton pump inhibitor - bismuth) is superior to an alternative proton pump inhibitor -based triple therapy (Nash et al., 2003). Monotherapy is not encouraged due to lack of efficacy and potential development of resistance (Hardin and Wright, 2002). Despite this range of

antibiotics, resistance has unfortunately emerged to most of them (Ndip et al., 2008; Tanih et al., 2010c) and is a major cause of treatment failure. Resistance of *H. pylori* to antibiotic treatment regimens is really a growing problem (Kwon et al., 2001; Nahar et al., 2004) and in several African countries is largely linked to misuse of antibiotics (Ndip et al., 2008). Resistance of the organism against clarithromycin and metronidazole resistance against this organism is common in many countries (Kwon et al., 2001; Tanih et al., 2010c), whilst resistance to different antibiotics used as first-line treatment varies between countries and communities, and may change with time, patient's age, sex, type of disease and geographical location (Tanih et al., 2010c).

In South Africa, the treatment regimen for *H. pylori* infection comprises amoxicillin, metronidazole, clarithromycin and doxycycline (Tanih et al., 2010c) and theoretically should demonstrate 85 to 95% efficacy (Tanih et al., 2010c). A study conducted by Jaskiewicz et al. (1993) demonstrated that treatment with omeprazole; 20 mg/day for one month followed by triple therapies (metronidazole, 400 mg three times a day, tetracycline, 500 mg four times a day with either colloidal bismuth, 120 mg four times a day or sucralfate 1 g four times a day) offer significant recovery in non-healing or recurrent duodenal ulcers patients. Also, lansoprazole and pantoprazole-based triple therapy, with either 1 or 2 weeks of co-therapy with amoxicillin and clarithromycin, is effective in eradicating *H. pylori* and healing duodenal ulceration (Louw et al., 1998).

In a recent study employing a phenotypic based method by Tanih et al. (2010c) in the Eastern Cape Province of South Africa, *H. pylori* strains were markedly susceptible to ciprofloxacin (100%) and amoxicillin (97.5%). Good activity was also reported for clarithromycin (80%) and gentamicin (72.5%). Susceptibility recorded for other antibiotics included 67.5% tetracycline, 55.5% to erythromycin and only 4.5% to metronidazole. In another study using the GenoType® Helico DR assay, 10.3% resistance was reported for the fluoroquinolone (Tanih and Ndip, 2013) as opposed to the 0% resistance previously reported to ciprofloxacin. The observed difference could be attributed to differences in strains as well as the methods (phenotypic versus molecular) used in both studies. However, fluoroquinolones has rarely been incorporated in the treatment regimen in South Africa (personal communication).

SURROGATES TO CIRCUMVENT RESISTANCE

The growing resistance of *H. pylori* to antibiotics used in its treatment alongside other inherent limitations of the triple therapy has brought forth the quest for surrogates' treatment from natural sources. Resistance of *H. pylori* is increasing and strains in South Africa are no exceptions (Ndip et al., 2008; Tanih et al., 2010c). A non-antibiotic approach to the treatment and prevention of these infections includes the application of plant and honey (Ndip et al., 2007a; 2007b; Manyi-Loh et al., 2010; Njume et al., 2011a;). Plant based treatment has offered significant lead in the management of intractable infectious diseases, including opportunistic acquired immunodeficiency syndrome (AIDS) infections (Klos et al., 2009; Otang et al., 2012). Herbal product usage in medicinal benefits has played an important role in nearly every culture on earth (Osinubi, 2008; Klos et al., 2009) with plants providing natural blueprints for the development of new drugs (Iwu et al., 1999) which may improve chemotherapeutic results (Klos et al., 2009). Novel and potentially important antibiotic prototype have been found in higher plants (plant extract and plant products) that have been screened for antimicrobial activity (Ndip et al., 2007b).

Herbal medicine has been widely used, and still forms an integral part of healthcare in most countries in the world (Desta, 1993; Anesini and Perez, 1993). An estimated 3.5 million people in developing countries rely on plant-based medicine for their primary healthcare (Farnsworth et al., 1985; Sofowara, 1993). The demand by patient to use natural products such as plants based products for the management of recalcitrant infections is on the increase (Njume et al., 2011a). Herbal medicines remain a normal part of life for most South Africans, especially blacks. Traditionally used medicinal plants are prescribed by traditional healers (Tanih et al., 2009; Njume et al., 2011a). In South Africa, scientific literature is rich on plant based studies although limited studies exist on anti-*H. pylori* activity using plants. A number of plants in South Africa, belonging to various families, have been screened in the search for their anti -*H. pylori* potential.

Njume et al. (2011b) evaluated a number of plants including *C. molle*, *S. birrea*, *G. kola*, *A. amatymbica* and some *Strychnos* species for their anti-*H.pylori* activity. These plants were selected based on ethno medicinal uses in the treatment of gastritis, peptic ulcer and other *H. pylori*-associated morbidities in South Africa and other African countries. All the plant crude extracts tested demonstrated anti-*H. pylori* activity with zone diameters of inhibition between 0 and 38 mm. Also, Okeleye et al. (2010; 2011) in their studies in South Africa demonstrated anti-*H. pylori* activity using *B. micrantha* and *P. africanum*. Njume and co-workers further investigated the volatile constituent of the acetone extract of *S. birrea* (A. Rich.) Hochst which demonstrated significant anti-*H. pylori* activity when compared to the other plants (Njume et al., 2011c). An acetone extract of the stem bark was fractionated by column chromatography and the volatile constituents identified by GC-MS. Terpinen-4-ol was identified to be the primary active constituent with inhibitory activity similar to amoxicillin; however, the authors indicated that high levels of the toxic compounds pyrrolidine and naphthalene also identified in the plant fraction warrant cautious use of *S. birrea* in ethnomedicine (Njume et al., 2011c).

Apitherapy has shown promising effects as an alternative source of *H. pylori* treatment (Davis, 2005). The antimicrobial activity of honey and its ability to inhibit bacterial growth are now well documented, and honey has been successfully used on infections that do not respond to standard antiseptic and antibiotic therapy (George and Cutting, 2007). Furthermore, the observation that honey in New Zealand and Saudi Arabia at concentrations approximating 20% v/v can inhibit the growth of *H. pylori in vitro*, grounded with the fact that Medihoney™ and manuka honeys have *in vivo* activity against ulcers, infected wounds and burns are significant findings which merits further and extensive investigations (Davis, 2005).

Reports exist on the beneficial effects of honey when used as an antiseptic for wounds, burns and ulcers, improving the assimilation of calcium and magnesium and decreasing acidity (Zaghloul et al., 2001; Ndip et al., 2007a). Stimulation of inflammatory- cytokine production by monocytes is likely the mechanism by which wounds are healed with the use of honey (Tonks et al., 2003). These encouraging observations have motivated scientists to investigate the activities of honeys further. Some investigators had previously reported that the activity of honey varies between types (Basualdo et al., 2007). The osmotic effect of honey, its naturally low pH, and the presence of hydrogen peroxide, phenolic acids, lysosomes and flavanoids in honey are all thought to help inhibit bacterial growth when honey is applied to a wound. Honey does not only contain sugars but also an abundance of minerals, vitamins, enzymes and amino acids (Tanih et al., 2009).

In South Africa, there is a dearth of studies related to the anti- *H. pylori* activity of honey. Recently, Manyi-Loh et al. (2010) investigated the anti -*H. pylori* activity of three local honeys; Pure honey, citrus blossom and goldcrest at four different concentrations [10, 20, 50 and 75 (% v/v)] as well as their solvent extracts (n-hexane, diethyl ether, chloroform and ethyl acetate) using the agar well diffusion method. All the honey varieties and their solvent extracts demonstrated varying levels of anti-*H. pylori* activity at concentrations ≥ 10% with different mean zone diameters of inhibition [16.0mm (crude) to 22.2mm (extract)] and percentage susceptibilities [73.3% (crude) to 93.3% (extract)] of the test isolates. The chloroform extract of Pure honey recorded MIC50 and MIC90 ranges of 0.01-10 and 0.625-10% (v/v), respectively; that were not significantly different (P>0.05) from amoxicillin (0.001-1.25mg/mL), the positive control. Based on this, it was concluded that, honeys (crude) and solvent extracted honey possess potential compounds with therapeutic activity which could be exploited further as lead molecules in the treatment of *H. pylori* infections (Manyi-Loh et al., 2010). Chemical analysis of the chloroform extract of the Pure honey led to the identification of 24 volatile compounds belonging to known chemical families present in honey. Astoundingly, thiophene and N-methyl-D3-aziridine were identified as novel compounds (Manyi-Loh et al., 2011).

CONCLUSION

Although *H. pylori* presents a tremendous challenge as a significant cause of gastric related morbidities, a dearth of knowledge on its prevalence, epidemiology and antimicrobial chemotherapy exist in South Africa. There is need therefore to embark on more studies to highlight the clinical and epidemiological significance of this pathogen in the country.

ACKNOWLEDGEMENT

We are grateful to the Govan Mbeki Research and Development Centre, University of Fort Hare, South Africa for funding.

REFERENCES

Ahmed K, Farzana R, Walter M, Godfrey L, Martin H (2007). Histopathological profile of gastritis in adult patients seen at a referral hospital in Kenya. World. J. Gastroenterol. 14:4117- 4121.

Ally R, Mitchell HM, and Segal I. (1999). Cag- A positive *H. pylori* aplenty in South Africa: the first systemic study of *H. pylori* infection in asymptomatic children in Soweto. Gut. 45(111):A97-8.

Anesini C, Perez C (1993). Screening of plants used in Argentine folk medicine for antimicrobial activity. J. Ethnopharmacol. 39:119-128.

Baako BN, Darko R (1996). Incidence of *H. pylori* infection in Ghanian patients with dyspeptic symptoms referred for upper gastrointestinal endoscopy. West Afr. J. Med. 15(4):223-227.

Basualdo C, Sgroy V, Finda MS, Marioli JM (2007). Comparison of the antibacterial activity of honey from different provenance against bacteria usually isolated from skin wounds. Vet. Microbiol.124:375-381.

Brown LM (2000). *H. pylori*: Epidemiology and routes of transmission. Epidemiol. Rev. 22(2):283-297.

Davis C (2005). The Use of Australian Honey in Moist Wound Management. Publication No. W05/159. Kingston, Australia: Rural Industries Research and Development Corporation.

Delport W, Cunningham M, Olivier B, Preisig O, van der Merwe SW (2006). A population genetics pedigree perspective on the transmission of *H. pylori*. Genetics. 174(4):2107-18.

Desta B (1993). Ethiopian traditional herbal drugs. Part II. Antimicrobial activity of 63 medicinal plants. J. Ethnopharmacol. 39:129-139.

Dube C, Nkosi TC, Clarke AM, Mkwetshana N, Green E, Ndip RN (2009b). *H. pylori* in an asymptomatic population of Eastern Cape Province, South Africa: Public health implication. Rev. Environ. Health. 24(3):249-255.

Dube C, Tanih NF, Ndip RN (2009a). *H. pylori* in water sources: a global environmental health concern. Rev. Environ. Health. 24(1):1-14.

Eslick GD (2000). Helicobacter pylori infection transmitted sexually via oral-genital contact: a hypothetical model. Sex Transm Infect. 76(6):489-92.

Eslick GD (2002) . Sexual transmission of *H. pylori* via oral-anal intercourse. Int J STD AIDS. 13(1):7-11.

Farnsworth NR, Akerele O, Bingel AS (1985). Medicinal plants in therapy. Bull. WHO. 63:965-981.

Fox JG, Batchelder M, Marini R, Yan L, Handt L, Li X, Shamen B, Hayward A, Campbell J, Murphy JC (1995). *H. pylori* induced gastritis in the domestic cats. Infect. Immun. 63(7): 2674-2681.

Fritz EL, Slavik T, Delport W, Olivier B, van der Merwe SW (2006). Incidence of Helicobacter felis and the effect of coinfection with *H. pylori* on the gastric mucosa in the African population. J. Clin Microbiol. 44(5):1692-6.

George NM, Cutting KF (2007). Antibacterial honey (Medihoney): in-vitro activity against clinical isolates of MRSA, VRE and other multiresistance Gram-negative organisms, including Pseudomonas aeruginosa. Wounds. 19:231-236.

Goosen C, Theron J, Ntsala M, Maree FF, Olckers A, Botha SJ, Lastovica AJ, van der Merwe SW (2002). Evaluation of a novel heminested PCR assay based on the phosphoglucosamine mutase gene for detection of *H. pylori* in saliva and dental plaque. J. Clin. Microbiol. 40(1):205-9.

Hardin FJ, Wright RA (2002). *H. pylori*: review and update. Hosp Phys. 38:23-31.

Holcombe C (1992*). H. pylori*: the Africa enigma. Gut. 33:429-431.

Iwu MW, Duncan AR, Okunji CO (1999). New antimicrobials of plant origin. In: Perspectives on New Crops and New Uses, ed. Janick, J. pp. 457-462.

Jaskiewicz K, Louw JA, Marks IN (1993). Local cellular and immune response by antral mucosa in patients undergoing treatment for eradication of *H. pylori*. Dig. Dis. Sci. 38(5):937-43.

Kalach N, Benhamou PH, Campeotto F, Bergeret M, Doupont C, Raymond J (2001). Clarithromycin resistance and eradication of *H. pylori* in children. Antimicrob. Agents Chemother. 45:2134-2135.

Kast RE (2007). Some fibrocystic breast change may be caused by sexually transmitted *H. pylori* during oral nipple contact: supporting literature and case report of resolution after gut *H. pylori* eradication treatment. Med Hypotheses.;68(5):1041-6.

Kawakami Y, Oana K, Hayama M, Ota H, Takeuchi M, Miyashita K, Matsuzawa T, Kanaya, K (2006). *In vitro* bactericidal activities of Japanese rice-fluid against Helicobacter pylori strains. Int. J. Med. Sci. 3:112–116.

Kidd M, Lastovica AJ, Atherton JC, Louw JA (1999b). Heterogeneity in the Helicobacter pylori vacA and cagA genes: association with gastroduodenal disease in South Africa? Gut. 45(4):499-502.

Kidd M, Louw JA, Marks IN (1999a). *H. pylori* in Africa: observations on an 'enigma within an enigma'. J. Gastroenterol. Hepatol. 14(9):851-8.

Kidd M, Peek RM, Lastovica AJ, Israel DA, Kummer AF, Louw JA (2001). Analysis of iceA genotypes in South African Helicobacter pylori strains and relationship to clinically significant disease. Gut. 49(5):629-35.

Klos M, van de Venter M, Milne PJ, Traore HN, Meyer D, Oosthuizen V (2009). In vitro anti-HIV activity of five selected South African medicinal plant extracts. J. Ethnopharmacol.15; 124(2):182-8.

Kwon DH, Hulten K, Kato M, Kim JJ, Lee M, El-Zaatari FAK, Osato MS, Graham DY (2001). DNA sequence analysis of rdxA and frxA from 12 pairs of metronidazole-sensitive and –resistant clinical *H. pylori* isolates. Antimicrob. Agents Chemother. 45:2609-2615.

Logan RPH, Walker MM (2002). Epidemiology and diagnosis of Helicobacter pylori infection. In: ABC of Upper Gastrointestinal Tract. Logan, R.P.H., Harris, A, Misiewicz, J.J., Baron, J.H. (eds).BMJ books. London pp.16-18.

Louw JA, Jaskiewicz K, Girdwood AH, et al. (1993). Helicobacter pylori prevalence in non-ulcer dyspepsia: ethnic and socio-economic differences. S. Afr. Med. J. 83(3):169-171.

Louw JA, Kidd MS, Kummer AF, Taylor K, Kotze U, Hanslo D (2001). The relationship between Helicobacter pylori infection, the virulence genotypes of the infecting strain and gastric cancer in the African setting. Helicobacter. 6(4):268-73.

Louw JA, van Rensburg CJ, Hanslo D, Grundlings HD, Girdwood AH, Marks IN (1998). Two-week course of pantoprazole combined with 1 week of amoxicillin and clarithromycin is effective in *H. pylori* eradication and duodenal ulcer healing. Aliment. Pharmacol. Ther. 12(6):545-50.

Louw JA, Zak J, Lucke W, Le Roux E, Jaskiewicz K, Winter T, Lastovica A, Marks IN (1992). Triple therapy with sucralfate is as effective as triple therapy containing bismuth in eradicating *H. pylori* and reducing duodenal ulcer relapse rates. Scand. J. Gastroenterol Suppl. 191:28-31.

Manyi-Loh CE, Clarke AM, Ndip RN (2011). Identification of volatile compounds in solvent extracts of honeys produced in South Africa. Afr. J. Agric. Res. 6(18) :4327-4334.

Manyi-Loh CE, Clarke AM, Munzhelele T, Green E, Mkwetshana NF, Ndip RN. (2010). Selected South African honeys and their extracts possess *in vitro* anti-*H. pylori* activity. Arch. Med. Res. 41:324-331.

Mosane TW, Malope B, Ratshikhopha ME, Hiss DC, Sitas F (2004). Seroprevalence of *H. pylori* IgG antibodies in South African mothers and their children. Eur. J. Gastroenterol. Hepathol. 16(1):113-114.

Nahar S, Mukhopadhyay AK, Khan R, et al. (2004). Antimicrobial susceptibility of *H. pylori* strains isolated in Bangladesh. J. Clin. Microbiol. 42:4856-4858.

Nash C, Fischbach L, Veldhuyzen van Zanten S. (2003). What are the global response rates to Helicobacter pylori eradication therapy? Can. J. Gastroenterol. 17 Suppl B:25B-29B.

Ndip RN, Malange AE, Akoachere JFT, Mackay WG, Titanji VPK, Weaver LT (2004). Helicobacter pylori antigens in the faeces of asymptomatic children in the Buea and Limbe health districts of Cameroon: a pilot study. Trop. Med. Inter. Health. 9:1036-1040.

Ndip RN, Malange- Takang AE, Echakachi CM, Malongue A, Akoachere J-F. T. K, Ndip LM, Luma HN (2007a). In-vitro antimicrobial activity of selected honeys on clinical isolates of *H. pylori*. Afr. Health Sci.7:228-231.

Ndip RN, Malange Tarkang AE, Mbullah SM, Luma HN, Malongue A, Ndip LM, Nyongbela K, Wirmum C, Efange SMN (2007b). *In- vitro* anti-Helicobacter pylori activity of extracts of medicinal plants from North West Cameroon. J. Ethnopharmacol . 114:452-457

Ndip RN, Takang MEA, Ojongokpoko AEJ, Luma HN, Malongue A, Akoachere KTJ-F, Ndip LM, MacMillan M, Weaver TL (2008). *H. pylori* isolates recovered from gastric biopsies of patients with gastroduodenal pathologies in Cameroon: Current status of antibiogram. Trop. Med. Inter. Health 13(6):848-854.

NIH consensus Development Panel on *H. pylori* in peptic ulcer disease. Helicobacter in peptic ulcer disease (1994). JAMA 272:65-69.

Njume C, Afolayan AJ, Green E, Ndip RN (2011c). Volatile compounds in the stem bark of *Sclerocarya birrea* (Anacardiaceae) possess antimicrobial activity against drug-resistant strains of *H. pylori*. Int. J. Antimicrob. Agents. 38(4):319-24.

Njume C, Afolayan AJ, Ndip RN (2011a). Diversity of plants used in the treatment of Helicobacter pylori associated morbidities in the Nkonkobe municipality of the Eastern Cape province of South Africa. J. Med. Plts Res. 5(14):3146 -3151.

Njume C, Afolayan AJ, Ndip RN (2011b). Aqueous and organic solvent-extracts of selected South African medicinal plants possess antimicrobial activity against drug-resistant strains of *H. pylori*: Inhibitory and bactericidal potential. Int. J. Mol. Sci. 12:5652-5665.

O'keefe SJ, Salvador B, Nainkin J, Majiki S, Stevens H, Atherstone A (2000). Empiric treatment based on *H. pylori* serology cannot substitute for early endoscopy in the management of dyspeptic rural black Africans. S. Afr. Med. J. 90:1129-1135.

Okeleye BI, Bessong PO, Ndip RN (2011) Preliminary phytochemical screening and *in- vitro* anti-*H. pylori* activity of extracts of the stem bark of Bridelia micrantha (Hochst., Baill., Euphorbiaceae). Molecules. 25; 16(8):6193-205.

Okeleye BI, Samie A, Bessong PO, Mkwetshana NF, Green E, Clarke AM, Ndip RN (2010). Crude ethyl acetate extract of the stem bark of *Peltophorum africanum* (Sond, Fabaceae) possessing in- vitro inhibitory and bactericidal activity against clinical isolates of *H. pylori*. J. Med. Plts Res. 4(14):1432-1440.

Olivier BJ, Bond RP, van Zyl WB, Delport M, Slavik T et al. (2006). Absence of *H. pylori* within the oral cavity of a South African community. J. Clin. Microbiol. 44:635-636.

Osinubi AA (2008). Effects of Vernonia amygdalina and chlorpropamide on blood glucose. Med. J. Islamic World Acad. Sci. 16:115-119.

Otang WM, Grierson DS, Ndip RN (2012). Phytochemical studies and antioxidant activity of two South African medicinal plants traditionally used for the management of opportunistic fungal infections in HIV/AIDS patients. BMC Complement. Altern. Med. 12:43

Pelsar HH, Househam KC, Joubert G, van der Linde G, Kraaj P, Meinardi M (1997). Prevalence of Helicobacter pylori antibodies in children in Bloemfontein, South Africa. J. Pediatr. Gastroenterol. Nutr. 24(2):135-139.

Samie A, Obi CL, Barrett LJ, Powell SM, Guerrant RL (2007). Prevalence of Campylobacter species, *H. pylori* and Arcobacter species in stool samples from the Venda region, Limpopo, South Africa: Studies using molecular diagnostic methods. J. Infect. 54:558-566.

Segal I, Ally R, Mitchell H (2001). *H. pylori*: an African perspective. Q. J. Med. 94:561-565.
Sofowara A (1993). Medicinal plants and traditional medicine in Africa, 4th Edn. Ibadan, Nigeria: Spectrum Books
Tanih NF, Dube C, Green E, Mkwetshana N, Clarke AM, Ndip LM, Ndip RN (2009). An African perspective on *H. pylori*: prevalence of human infection, drug resistance, and alternative approaches to treatment. Ann. Trop. Med. Parasitol. 103(3):189-204.
Tanih NF, Okeleye BI, Naidoo N, Green E, Mkwetshana N, Clarke AM, Ndip, LM, Ndip RN (2010a). *H. pylori* prevalence in dyspeptic patients in the Eastern Cape Province of South Africa: ethnicity and disease status. S. Afr. Med. J. 100:734-737.
Tanih NF, McMillan M, Naidoo N, Ndip LM, Weaver LT, Ndip RN (2010b). Prevalence of *H. pylori* vacA, cagA and iceA genotypes in South African patients with upper gastrointestinal diseases. Acta Tropica. 116:68-73.
Tanih NF, Okeleye BI, Naido N, Clarke AM, Mkwetshana N, Green E, Ndip LM, Ndip RN (2010c). Marked susceptibility of South African *H. pylori* strains to ciprofloxacin and amoxicillin: Clinical implication. S. Afr. Med. J. 100(1):49-52.
Tanih NF, Ndip RN (2013). Molecular detection of antibiotic resistance in South African isolates of *H. pylori*. Gastroenterol. Res. Pract. 2013: 259457. doi:10.1155/2013/259457
Thomas JE, Dale A, Bunn JE, Harding M, Coward WA, Cole TJ, Weaver LT (2004). Early *H. pylori* colonisation: the association with growth faltering in the Gambia. Arch. Dis. Child. 89(12):1149-1154.
Tkachenko MA, Zhannat NZ, Erman LV, Blashenkova EL, Isachenko SV, Isachenko OB, Graham DY and Malaty HM (2007). Dramatic changes in the prevalence of *H. pylori* infection during childhood: a 10-year follow-up study in Russia. J. Pediatr. Gastroenterol. Nutr.45 (4):428-432.
Tonks AJ, Cooper RA, Jones KP, Blair S, Parton J, Tonks A (2003). Honey stimulates inflammatory cytokine production from monocytes. Cytokine.721:242-247.
Wirth T, Wang X, Linz B, Novick RP, Lum JK, Blaser MJ, Morelli G, Falush D, Achtman M (2004). Distinguishing human ethnic groups via sequences from *H. pylori* lessons from Ladakh. Proc. Natl. Acad. Sci . 101: 4746-4751.
Zaghloul AA, Shattawy HHE, Kassem AA, Reddy IK, Khan MA (2001). Honey, a prospective antibiotic: extraction, formulation, and stability. Pharmazie. 56:643-647.