Prevalence of malaria and *Helicobacter pylori* Coinfection associated with sociodemographic characteristic among blood donors in Douala General Hospital.

Comment [H1]: RECAST PREVALENCE OF MALARIA AND HELIPCOBACTER PYLORI COINFECTION AND ASSOCIATED SOCIODEMOGRAPHIC FACTORS AMONG DONORS IN DOUALA GENERAL HOSPITAL

ABSTRACT

Background: The malaria parasite *Plasmodium* is intra-erythrocyte hence can be transmitted by transfusion of any blood component containing infected red blood cells. *Helicobacter pylori* infection affects more than half of the human population worldwide. Infection remains asymptomatic in most individuals, although some individuals develop acute gastritis, peptic or duodenal ulcers, gastric cancer, and mucosa associated tissue lymphoma. *H. pylori* infection have been implicated in some haematological manifestations such as anaemia and micronutrient deficiency.

Objective: This research was designed to determine the prevalence of malaria parasitaemia and *H. pylori* coinfection in association with sociodemographic characteristics among donors in Douala General Hospital.

Methodology: The study was a hospital-based study carried out from January to May 2022. The study population comprised of 106 donors who came to the hospital laboratory for blood donation. A structured questionnaire was used to get demographic and clinical data. Two ml of blood was collected from individuals to prepare a thick and thin blood film for malaria parasite determination and to centrifuge at 3000 rpm for 5minutes to obtain plasma for *H. pylori* test strip.

Results and Discussion: The overall prevalence of *H. pylori* in the study area was 70.8%. The female donors had a prevalence of 72.0%. A greater proportion of blood group O donors had *H. pylori* than groups A, AB and B but this difference was not significant (P-value = 0.571). The prevalence of malaria parasites infection was 36.8%. Those of blood group A had a higher prevalence rate of 42.3% (11/26). Out of the 106 donors, 23 (21.7%) had malaria and *H. pylori* coinfection. 68 (64.2%) donors had a mono-infection that is either having malaria mono-infection or *H. pylori* mono-infection and 15 (14.2%) had no infection. Malaria and *H. pylori* coinfection was higher in female donors than males (OR = 1.059, 95% Cl 0.359 -3.119, P =0.917), in donors aged below 25 years old (OR = 0.338, 95% Cl 0.075 - 1.535, P =0.160), replacement donors (OR = 1.350, 95% Cl 0.460 – 3.964, P =0.585); blood donors of blood group AB (OR = 0.654, 95% Cl 0.181 – 2.366, P =0.517) and Rhesus negative donors (OR = 1.500, 95% Cl 0.130 – 17.36, P =0.746).

Conclusion: The prevalence of *H. pylori* infection and Malaria among blood donors in Douala General Hospital were high and coinfection was higher in females than males. Both malaria parasites and *H. pylori* infections have been implicated in blood parameters such as anaemia and micronutrient deficiency. It is therefore recommended that routine screening for malaria parasites and *H. pylori* be done in blood banks before transfusion for a high blood quality.

Comment [H2]: RECAST ACCORDING TO JOURNAL GUIDELINES REDUCE TO 300 WORDS

Keys Words: Malaria parasites, *Helicobacter pylori*, blood donors, Cameroon.

Introduction

Malaria is endemic in Africa and remains the most complex and overwhelming health problem facing humanity in the tropical and subtropical regions of the world. It accounts for most deaths in these regions especially in children below the age of 5 years [1]. In malaria-endemic areas, epidemiological studies have reported a prevalence of malaria among potential blood donors to range between 1% and > 50% [2;3]. Plasmodium species may live in the donors for years without causing any symptoms and donors from highly malaria endemic areas who have acquired relative malarial immunity may have asymptomatic parasitaemia that can persist for varying periods depending on species [4]. The malaria parasite plasmodium is intraerythrocytic hence can be transmitted by transfusion of any blood component containing infected red blood cells. Transfusion- transmitted malaria compared to natural malaria has a short incubation period because there is no pre-erythrocytic development and depends on the species of parasite introduced which varies from 10 days in *P. falciparum* to 40 days or longer in *P. malariae*. The risk of transfusion-transmitted malaria however differs widely among low endemic countries, where the imported infection occurs in individuals that have travelled to or migrated from endemic regions. It is therefore important that the possibility of donors from malaria prone environment transmitting the parasite through blood donation is examined thoroughly [5].

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H. pylori infection affects more than half of the human population worldwide. Infection remains asymptomatic in most individuals, although some individuals develop acute gastritis, peptic or duodenal ulcers, gastric cancer, and mucosa associated tissue lymphoma. High prevalence of *H. pylori* infection (70%-90%) is found among persons in developing countries [6] but, about 20% of *H. pylori* infected people develop clinically apparent conditions such as peptic ulcers or neoplasia. Furthermore, *H. pylori* infection has been implicated in some haematological manifestations such as anaemia and micronutrient deficiency (iron, and vitamin B12) [7,8]. These micronutrients play a key role for haemoglobin synthesis and maturation of red blood cells.

In Cameroon, like in most other endemic regions blood transfusion policy makes no mention of screening donated blood for malaria or of treating recipients prophylactically, blood is not routinely screened for malaria and coinfection, so the information on the prevalence of malaria parasitaemia and *H. pylori* infection among blood donors are limited. Therefore, this research

was designed to determine prevalence of malaria parasitaemia and *H. pylori* co-infection associated with sociodemographic characteristics among blood donors in Douala General Hospital

MATERIALS AND METHODS

Study area

The study was carried out at the Douala General Hospital, in the littoral region of Cameroon. Douala is the economic capital and main business centre in Cameroon, in Central Africa with a population of 3.7 million. The city develops from it trading port on the estuary of the Wouri River open to the Gulf of Guinea. The hospital has specialized service such as paediatrics, surgery, Laboratory, Gynaecology, Maternity, ophthalmological, oncology, optometry, HIV treatment centre, haemodialysis centre and other rehabilitation services

Study Design, Population and Duration

The study was a cross-sectional hospital-based study where information was collected from all participants who presented for donation at blood bank of the general hospital of Douala from January to May 2022.

Sample Population, Sampling Technique and Data Collection

Consenting individuals who came to donate blood (voluntary blood donors, replacement blood donors and commercial blood donors) at the Douala general hospital were recruited for this study. The blood pressure of the blood donors was measured using a blood pressure monitor, their weight was equally measured using a scale balance. Participants were sent to the counselling room and those whose parameters did not meet the hospital's eligibility criteria were rejected while donors who were eligible for donation were sent to the collection room. The donors were screened for viral infections such as Hepatitis B, C and HIV as per protocol. A designed questionnaire was administered to participants with sections of the socio-demographic characteristics, epidemiological and clinical data of participants such as age, gender; the type of donor and blood group type.

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Sample Size Calculation

The sample size determination was calculated using the Cochrane formula

$$n = \frac{Z^2 p(1-p)}{d^2}$$

Where:

n = sample size;

Z = 1.96, critical Z-value at 95% confidence interval;

p = 6.5%, prevalence of malaria parasitaemia in blood donors in Yaoundé [5]

d = 0.05, margin of error to be tolerated.

Substitution of the above, at least 93 participants were chosen

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Exclusion and inclusion criteria

All screened prospective voluntary donors who have given their consent to the study were included in this study; Donors who on anti-malarial drug treatment and antibiotic were excluded; Donors who have not accepted for their information to be accessed were not excluded. Informed consent was obtained from the participants. Participant's information was obtained and kept confidentially by not taking any of their personal information such as names; rather codes were assigned to each participant after data collection and each participant was given equal treatment.

Comment [H6]: REPEATITION OF THE PREVIOUS INFORMATION . PLEASE CHOOSE WHICH TO USE OR RECAST

Sample Collection and Test Procedure

Procedure for thick and thin film

Two ml of blood was collected from the patients into an EDTA tube using venepuncture technique. Few drops of blood were used and placed on the slides to prepare a thick and thin blood film for malaria parasitaemia and the slides were allowed to air dry. The remaining blood in the EDTA tube was then centrifuged at 3000 rpm for 5 minutes to obtain plasma. The *H. pylori* test (Onsite Rapid Test, CTK Biotech) strip was was used where 25µl of serum/plasma is placed vertically into the sample well of the cassette. Two drops (100µl) of the buffer were added and the results were read after fifteen minutes. Where the test line and the control lines appeared, the test was recorded as positive, but where just the control line appeared, the test was recorded as negative. The malaria slides were stained with Giemsa and observed using the oil immersion objective (X100), at least 10 fields were observed and the malaria parasites counted.

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Parasite densities were estimated by counting the number of asexual parasites (trophozoites) per 200 WBCs and converting to parasites/μl assuming a total WBC count of 8000/μl of blood [6].

Ethical Consideration

Administrative authorizations were obtained from the General Hospital of Douala and from the Faculty of Health Sciences, University of Buea. Informed consent was obtained from the participants. Participant's information was obtained and kept confidentially by not taking any of their personal information such as names; rather codes were assigned to each participant after data collection and each participant was given equal treatment.

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Data analysis

The Data was entered into Statistical Package for Social Sciences (SPSS), Chicago, IL, the USA for Windows, version 25. Data were analysed using descriptive statistics; this included the use of tables and percentages to explain the results. Bivariate and multivariate logistic regression analyses were performed to evaluate the association between variables and coinfection. Variables with a p-value < 0.05 from multivariable logistic regression was considered statistically significant.

RESULTS

Distribution of Study Participants

The 106 participants of this study were categorized with respect to their socio-demographic factors as shown in Table 1, the participants were in the age ≤ 25; 26 to 30; 31 to 35; 36 to 40 and > 40 years and representing a percentage of 26.4%; 21.7%; 24.5%; 16.0% and 11.3 % respectively with mean age of 21.2 ± 6.61. 76.4% of the participants were male while 23.6% were females. Majority of these blood donors had tertiary education as the highest level of education achieved with 51.9% while 30.2% and 17.9% of them had achieved secondary and primary education respectively. Twenty-seven (25.5%) of donors were unemployed and the most common proposal of the donation was for replacement as well as for commercial with 39.6% followed by and voluntary donation with 20.8%. Thirty-six (34.0%) of the blood donors were blood group O, 24(22.6%) blood group B, 26(24.5%) blood group A while 20(18.9%) were

blood group AB. Donors of rhesus positive accounted for 96.2% and those of rhesus negative were 3.8%.

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Table 1: Socio-demographic characteristics of the study population

Characteristic	Frequency (n= 106)	Percentage (%)
Gender		
Male	81	76.4
Female	25	23.6
Age (years)		
≤ 25	28	26.4
26 - 30	23	21.7
31 - 35	26	24.5
36 - 40	17	16.0
> 40	12	11.3
Total	**106**	**100**
Type of donor		
Replacement	42	39.6
Commercial	42	39.6
Voluntary	22	20.8
Total	**106**	**100**
Education		
Primary	19	17.9
Secondary	32	30.2
Tertiary	55	51.9
Total	**106**	**100**
Job		
Unemployed	27	25.5
Self-employed	39	36.8
Employed	40	37.7
Total	**106**	**100**
Blood group		
A	26	24.5
B	24	22.6
AB	20	18.9
O	36	34.0
Total	**106**	**100**
Rhesus		
Positive	102	96.2
Negative	4	3.8
Total	**106**	**100**

Prevalence of *Helicobacter pylori* associated with sociodemographic characteristic among blood donors in Douala General Hospital

Thirty-one (29.2%) of the participants were negative to *H. pylori* and 75 (70.8%) were positive. *H. pylori* infection was higher among males 57 (74%) than females 18 (24%).

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Table 2: Prevalence of *Helicobacter pylori* among blood donors in Douala General Hospital

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Parameter	Frequency	Percentage
Positive	75	70.8%
Negative	31	29.2%
Total	**106**	**100.0%**

The female donors had a higher prevalence rate of 72.0% (18/25) while that of male donors was 70.37% (57/81). However, there was no significant association between gender and prevalence of *H. pylori* infection (p=0.876). In relation to the age group, the highest prevalence rate of 82.4% (14/17) was obtained among donors aged above 40, while the least (64.3%, 18/28) was recorded in the age range 26 to 30 years. There was no significant association between age group and prevalence of malaria (P=0.599). Base on blood group, those of blood group O had a higher prevalence rate of 77.8% (28/36). Furthermore, there was no significant association between blood group and prevalence of *H. pylori* infection (p= 0.571). Job (P=0.560), Type of donor (P=0.752), education (P=0.469), and rhesus (P=0.849) on the other hand, did not impact significantly on the likelihood of having *H. pylori* infection (**Table 2)**.

Table 3: Prevalence of *H. pylori* associated with sociodemographic characteristic among blood donors in Douala General Hospital

Characteristic	Frequency	*H. pylori*		P-value
		Positive (%)	Negative (%)	
Gender				
Male	81	57 (70.4)	24 (29.6)	0.876
Female	25	18 (72.0)	7 (28.0)	
Age (years)				
≤ 25	28	18 (64.3)	10 (35.7)	
26 - 30	23	18 (78.3)	5 (21.7)	0.599
31 - 35	26	17 (65.4)	9 (34.6)	

36 - 40	17	14 (82.4)	3 (17.6)	
> 40	12	8 (66.7)	4 (33.3)	
Type of donor				
Replacement	42	31 (73.8)	11 (26.2)	
Commercial	42	28 (66.7)	14 (33.3)	0.752
Voluntary	22	16 (72.7)	6 (27.3)	
Education				
Primary	19	14 (73.7)	5 (26.3)	
Secondary	32	20 (62.5)	12 (37.5)	0.469
Tertiary	55	41 (74.5)	14 (25.5)	
Job				
Unemployed	27	17 (63.0)	10 (37.0)	
Self-employed	39	28 (71.8)	11 (28.2)	0.560
Employed	40	30 (75.0)	10 (25.0)	
Blood group				
A	26	18 (69.2)	8 (30.8)	
B	24	17 (70.8)	7 (29.2)	0.571
AB	20	12 (60.0)	8 (40.0)	
O	36	28 (77.8)	8 (22.2)	
Rhesus				
Positive	102	72 (70.6)	30 (29.4)	0.849
Negative	4	3 (75.0)	1 (25.0)	
Total	**106**	**31 (29.2)**	**75 (70.8)**	

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Prevalence of Malaria parasites infestation among blood donors in Douala General Hospital

The prevalence malaria was 36.8% (**Table 4)**.

Table 4: Prevalence of Malaria parasites among blood donors in Douala General Hospital

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	Frequency	Percentage
Positive	39	36.8%
Negative	67	63.2%
Total	106	100.0%

Prevalence of malaria associated with sociodemographic characteristic among blood donors in Douala General Hospital

The female donors had a higher prevalence rate of 44.0% (11/25) while the male donors had a lower prevalence rate of 34.6% (28/81). However, there was no significant association between gender and prevalence of malaria (P=0.393). In relation to the age group, the highest prevalence rate of 41.7% (5/12) was obtained among donors aged above 40, while the least (30.4%: 7/23) was recorded in the age range 26 to 30 years. There was no significant association between age group and prevalence of malaria (P=0.940). Base on blood group, those of blood group A had a higher prevalence rate of 42.3% (11/26). In addition, there was no significant association between blood group and prevalence of malaria (P= 0.587). Job (P=0.456), Type of donor (P=0.623), education (P=0.837), and rhesus (P=0.975) on the other hand, did not impact significantly on the likelihood of having Malaria infection (**Table 5)**.

Table 5: Prevalence of malaria parasites associated with sociodemographic characteristics among blood donors in Douala General Hospital

Characteristic	Frequency	*Malaria*		p-value
		Positive (%)	Negative (%)	
Gender				
Male	81	28 (34.6)	53 (65.4)	0.393
Female	25	11 (44.0)	14 (56.0)	
Age (years)				
≤ 25	28	11 (39.3)	17 (60.7)	
26 - 30	23	7 (30.4)	16 (69.6)	0.940
31 - 35	26	9 (34.6)	17 (65.4)	
36 - 40	17	7 (41.2)	10 (58.8)	
> 40	12	5 (41.7)	7 (58.3)	
Type of donor				
Replacement	42	14 (33.3)	28 (66.7)	
Commercial	42	15 (35.7)	27 (64.3)	0.623
Voluntary	22	10 (45.5)	12 (54.5)	
Education				
Primary	19	8 (42.1)	11 (57.9)	
Secondary	32	12 (37.5)	20 (62.5)	0.837
Tertiary	55	19 (34.5)	36 (65.5)	

Job				
Unemployed	27	10 (37.0)	17 (63.0)	
Self-employed	39	17 (43.6)	22 (56.4)	0.456
Employed	40	12 (30.0)	28 (70.0)	
Blood group				
A	26	11 (42.3)	15 (57.7)	
B	24	10 (41.7)	14 (58.3)	0.587
AB	20	8 (40.0)	12 (60.0)	
O	36	10 (27.8)	26 (72.2)	
Rhesus				
Positive	102	38 (37.3)	64 (62.7)	0.618
Negative	4	1 (25.0)	3 (75.0)	

Prevalence of malaria parasites and *H. pylori* Coinfection associated with sociodemographic characteristic among donors in Douala General Hospital

Out of the 106 donors, 23 (21.7%) had malaria and *H. pylori* coinfection. Sixty-eight (64.2%) donors had a mono-infection that is either having malaria mono-infection or *H. pylori* mono-infection 15 (14.2%) had no infection (**Figure 1).**

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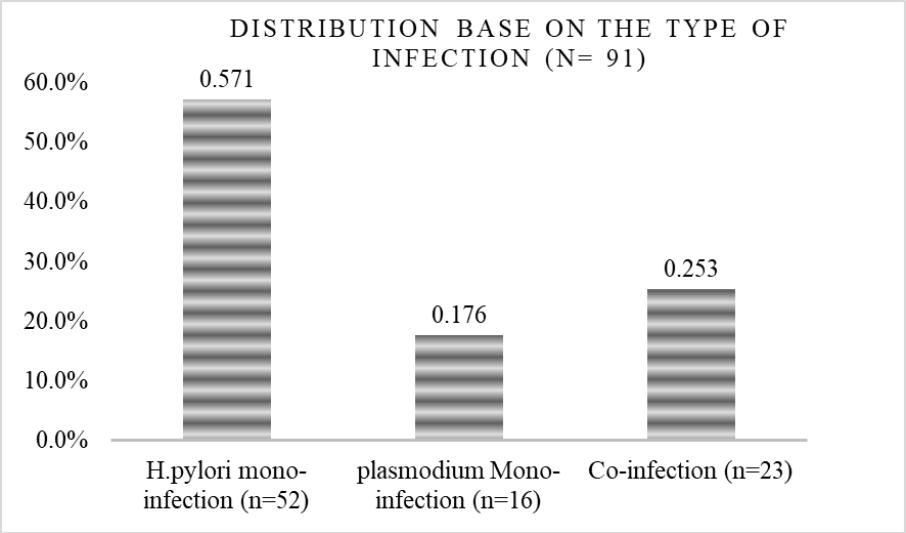

Figure 1: Distribution of mono and coinfection among blood donors in Douala General Hospital

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Factors associated with Malaria and *H. pylori* co-infection

Malaria and *H. pylori* coinfection was higher in female donors (26.1%), donors aged below 25 years old (31.8%), replacement donors (28.6%) blood donors of blood group AB (35.0%) and Rhesus negative patients (33.3%). However, no statistical significant difference was found (**Table 6**)

Table 6: Factors associated with Malaria and *H. pylori* co-infection

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Characteristic	Frequency	*Malaria and H. pylori co-infection (N=106)*		COR (95% Cl)	p-value
		YES (%)	NO (%)		
Gender					
Male	68	17 (25.0)	51 (75.0)	1	
Female	23	6 (26.1)	17 (73.9)	1.059 (0.359 -3.119)	0.917
Age (years)					
≤ 25	22	7 (31.8)	15 (68.2)	1	
26 - 30	22	3 (13.6)	19 (86.4)	0.338	0.160

				(0.075 - 1.535)	
31 - 35	21	5 (23.8)	16 (76.2)	0.670 (0.174 - 2.574)	0.559
36 - 40	16	5 (31.3)	11 (68.8)	0.974 (0.243 – 3.897)	0.970
> 40	10	3 (30.0)	7 (70.0)	0.918 (0.181 – 4.655)	0.918
Type of donor					
Replacement	35	10 (28.6)	25 (71.4)	1	
Commercial	35	8 (22.9)	27 (77.1)	1.350 (0.460 – 3.964)	0.585
Voluntary	21	5 (23.8)	16 (76.2)	1.055 (0.294 – 3.782)	0.935
Education					
Primary	16	6 (37.5)	10 (62.5)	1	
Secondary	26	6 (23.1)	20 (76.9)	0.500 (0.128 – 1.953)	0.319
Tertiary	49	11 (22.4)	38 (77.6)	0.482 (0.143 – 1.625)	0.239
Job					
Unemployed	21	6 (28.6)	15 (71.4)	1	
Self-employed	34	11 (32.4)	23 (67.6)	0.418 (0.135 – 1.299)	0.132
Employed	36	6 (16.4)	30 (83.3)	0.836 (0.255 – 2.745)	0.768
Blood group					
A	23	6 (26.1)	17 (73.9)	1	
B	16	4 (25.0)	12 (75.0)	1.526 (0.413 – 5.642)	0.527
AB	20	7 (35.0)	13 (65.0)	0.654 (0.181 – 2.366)	0.517
O	32	6 (18.8)	26 (81.3)	0.944 (0.218 – 4.088)	0.939
Rhesus					
Positive	88	22 (25.0)	66 (75.0)	1.500 (0.130 – 17.36)	0.746
Negative	3	1 (33.3)	2 (66.7)	1	

Discussion

The prevalence of malaria in donors at the Douala General hospital (DGH) was 42.9%. This result is in line with malaria prevalence related data in donors in Sub-Saharan Africa that range

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from 0.6% to 50% [10]. The prevalence observed in this study is also similar to a study conducted in Nigeria where the prevalence was 45.8% [11]. This high rate may be explained by the risk of exposure to malaria in urban area such as Douala. Also, there is a lack of interest by blood banks and blood donor to diagnose the infection before transfusion. The obtained prevalence was higher than that obtained by Koanga *et al.,* [12] and Okalla *et al.,* [13] who carried out similar studies at the DGH with slightly different study design and participant. The authors obtained 27.5% and 12.4% respectively among blood donors at the DGH. Again, our result was comparatively higher than other studies carried out in other localities in Cameroon [14, 15, 16] and foreign studies in Nigeria [17, 18], Ghana [19, 20] and Ethiopia [21]. The female donors were more infected by the malaria parasite than males (44.0%) as well as the participants aged above 40 years old (41.7%) and those of blood group A (42.3%). Gender, age group and blood group did not significantly affect the risk of malaria infection ($p>0.05$). This absence of association was similarly reported by other authors [22,23, 24]. The overall prevalence of *H. pylori* infection among the blood donors was 70.8% (75/106). This is in agreement with the prevalence of 77.2% and 69.5% reported previously by Khosravi et al., [25] and Sasidharan *et al.,* [26] respectively among blood donors. The obtained prevalence was higher than the 53% and 62.4% reported by Us *et al.,* [27] and Al-Balushi et al., [28] and respectively. This high prevalence for *H. pylori* infection in our setting could be due to lack of safe drinking water and lack of basic hygiene. Again, Douala been a cosmopolitan town overcrowded living conditions and poor diet could also explain this high prevalence.

The sero-positivity of *H. pylori* did not increase with age instead we observed a higher prevalence in donors aged below 24 years old than older donors, this high prevalence in younger adult was also reported by other authors [29, 30]. The high prevalence for *H. pylori* among the age group of below 24 years could be attributed to work related factors such as stress or academic related factors. In relation to ABO blood group type, the seroprevalence of *H. pylori* was higher in donors of blood group AB (40.0%), this finding is in accordance to that Tadesse *et al.,* [31] and in contradiction to several studies conducted in different countries where the O blood group was the most prevalent and the AB blood group was the least prevalent [26,32-33].

The prevalence of Malaria and *H. pylori* co-infection of both diseases among donors at the DGH was 21.7% which is higher than that of Nyanga *et al.,* [34] who obtain a 9.9% prevalence in

Buea, Cameroon. This difference in prevalence is probably due to greater sensitization on health issues, risk and prevention over the past few years. Considering that Douala is principally a big town with an overcrowded population compare to Buea and host people from different areas and countries, there is probably less sensitization on disease prevention. Furthermore, females had a higher prevalence of malaria and *H. pylori* co-infection than their male counterparts. This could be due to the fact that women performed more work related to the environment and soil than men, like farm work, night street vending and so may be more exposed to the two pathogens. Similar observation was made by Nyanaga *et al.* [34] with no significant statistical association between sex and prevalence of coinfection in both studies. Based on participants' education, it was observed that those who had primary education as their highest level of education had a high prevalence of *H. pylori* infection and malaria. This could be related to the fact that this group of participants are less expose to sensitization on health issues, risk and prevention. This reason could also explain the high prevalence of malaria and *H. pylori* coinfection in donors aged below 26 years old. As oppose to our study there was a statistical significant association between age and prevalence of malaria and *H. pylori* co-infection in a study conducted Nyanaga et al. [34], however the prevalence rate there was higher in patient above 40 years of aged.

Malaria and *H. pylori* coinfection was highest in replacement donors (28.6%) than the other type of donors, even though the difference was not statistically significant. Other authors have highlighted the similar observations. Bartonjo *et al*., 2019; [35] suggested that family replacement donor blood have higher sero-activity rates than voluntary donors and these may possibly due to a number of factors including high risk behaviours and paid donors posing as close family members or relatives. It is conceivable that a person in need of money is more likely to conceal his/her true state of health. Monetary motivation of donors might be highly appealing to people who live in desperate financial need. Hence these results strongly indicate that replacement donors are less suitable and major emphasis should be made to encourage voluntary non-remunerated blood donors. on the ABO blood grouping and rhesus factor, the prevalence rate of *H. pylori* and malaria coinfection was higher in donors of blood group AB and those of rhesus negative.

Conclusion

The prevalence of *H. pylori* and Malaria among blood donors in Douala General Hospital were high and coinfection was higher in female donors than males and in donors aged below 25 years old. Replacement donors had high prevalence compared to those commercial and voluntary donors. Blood donors of blood group AB and Rhesus negative donors also have the highest prevalence. However, no significant difference was found. It is therefore recommended that routine screening for malaria parasites and *H. pylori* be done in the blood banks before they are transfused to patients in the blood banks.

Data availability

The data that support the findings of this study are available on request from the corresponding author, [WD]

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