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COMPARATIVE STUDY OF HEPATITIS B INFECTION AND RELATED CO-INFECTIONS IN VOLUNTARY AND FAMILY REPLACEMENT BLOOD DONORS AT PORT MORESBY GENERAL HOSPITAL BLOOD TRANSFUSION SERVICE: A RETROSPECTIVE STUDY

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ABSTRACT:
This retrospective study was carried out at the Blood Transfusion Service in Port Moresby General Hospital, which is a teaching and specialist Hospital in the National Capital District Papua New Guinea. The aim of this study was to statistically assess if family replacement blood donors pose a higher risk of transmission of infection than voluntary donors. For every 10 voluntary donors who donated blood each month from 2010-2014, 10 family replacement donors were randomly selected and analysed retrospectively using data from archived record books. The Chi-square test was used to compare the infection difference in the two populations and odds ratio was also calculated. No statistically significant differences in HIV and syphilis infections were obtained between the two blood donor groups, though the risk of voluntary donors being infected with the HIV was high (OR 1.1579, 95%CI 0.8125-1.6502). However, statistically significant difference existed in HBV infection, with all donors positive for HBV were found among Family replacement donors. Our data indicated that family replacement donation should not be completely discouraged especially in settings where there are acute shortages of blood supply.

Keywords: Voluntary Donors, Family Replacement Donors, Hepatitis B Virus, Human Immunodeficiency Virus, Syphilis.

INTRODUCTION:

Hepatitis B is the most common liver infection in the world and is caused by the hepatitis B virus (HBV) [1]. It affects approximately 2 billion people worldwide, three quarters of which are chronic carriers and are found in Asia and the Western Pacific region [1]. Countries like Africa, Asia and the Western Pacific region have high HBV prevalence (> 8%), Southern and Eastern Europe have prevalence of 2-7% (intermediate), while Western Europe, North America and Australia have low prevalence [1]. In areas of high prevalence, the mode of transmission is mainly vertical; from mother to child during child birth. A study on women of child-bearing-age in Papua New Guinea (PNG) revealed that 85% of them had markers to the HBV, 37% tested positive for the HBsAg, while

6.6% tested positive for the e- antigen (HBsAg) [2]. About 90% of the cases were acquired perinatally as compared to areas with low prevalence where acquisition was mainly through unprotected sex and drug abuse [3]. In countries with intermediate prevalence rate, the virus may be acquired mainly through horizontal means [4]. During childhood, children are very active and therefore the virus can be spread through cuts or open sores on the skin, sharing of chewing gum, tooth brush and towels especially in developing countries [4]. Several studies have reported that the virus can also be transmitted through contaminated human blood and blood products during transfusion [5-8].

Other pathogens that can be detected in blood and its products and also transmitted mostly through sexual contacts are *Trepanoma pallidum* (TP), the bacteria that causes syphilis, and also the Human immunodeficiency virus (HIV). In PNG, there has been no documented case of blood transfusion transmission of the HIV; although an average of 15% blood donors have been demonstrated to be positive for HBV [9]. Since then, there has not been any published article on the HBV prevalence in blood donors nationwide. However, according to a poster abstract published by the Official Journal of the Australasian College of Tropical Medicine (ACTM) in July 2011, an overall HBV prevalence of 25.4% (95%CI 24.49-26.26%) was demonstrated in blood donors from East New Britain Province, Papua New Guinea [10].

Blood and its products are not manufactured, but donated by people who either voluntarily (voluntary donors) donate it to someone in need or are paid to give their blood to someone in need. Family members or relatives (family replacement donors) also give their blood to help a relative or family member, or even a close friend. Blood and its products have many clinical applications. In PNG, the need for blood for patient care is very high but the availability is very limited [11]. The country has also been reported to be facing acute shortages of blood in all the major provincial and district hospitals in 2015 [12].

Provision of safe blood to those in need is therefore the norm of every blood bank transfusion services in PNG and elsewhere. It is now well documented by the World Health Organization (WHO) that voluntary donation is safer than family replacement in most parts of the world [13]. In the United States of America (USA), transmission of the hepatitis B virus through blood transfusion has decreased owing to adequate blood screening and exclusion of paid blood donors [1]. The same scenario is also seen in many other European countries [14]. These countries have taken initiatives to promote voluntary and unpaid donations through information campaigns, students' awareness and setting aside or making use of special days to promote voluntary blood donation [14]. In PNG, the Manager for PNG Blood Transfusion Services have used social media such as FaceBook and "Radio Talk

Back" show on 100FM to help save a life by donating blood and also to thank those voluntary donors who have been faithfully donating regularly [12].

In PNG, it is possible that some sections of the population are unaware of blood borne diseases, due to lack of awareness. Blood bank centres throughout the country continue to face acute shortages of blood supply [12] and therefore quite often family members are asked to donate. Based on the findings reported by the WHO [13], if family members continue to be the major blood donors for their relatives it is more likely that the risk of transmission of infection to recipients may remain high. In PNG there are no published data comparing the prevalence of infection among voluntary and family replacement blood donors. Therefore, this study was carried out to statistically assess if family replacement blood donors in this setting pose a higher risk of transmission of infection than that of voluntary donors.

METHODS:

A retrospective study was done using archived blood transfusion data records at Port Moresby General Hospital Blood transfusion service (PMGHBTS) from 2010 to 2014. Blood donors from all walks of life donate blood in the PMGHBTS because it is situated in the National Capital District (NCD) which is the capital city of PNG. Data collection from the archived records was carried out systematically. For every first 10 voluntary donors (VD) for every month of each year in the period studied, 10 family replacement donors (FRD) were also recorded. Other parameters collected were date of donation, age, gender, employment status, donor status (old or new donors), infection status (HBV, HIV & Syphilis) and donation type (voluntary or family replacement). All data were recorded onto Microsoft Excel Spreadsheet (version 2010).

Chi-square test was used to compare the data; Fishers Exact test was used where sample populations were small. Level of significance was set at 0.05. Qualitative data were described in numbers and percentages. The odds of each group of donor type being infected by any of the three pathogens were calculated using Odds ratio (OR) statistics. Confidence interval (CI) was also calculated to ensure the CI will contain the true OR. Ethical clearance and permission for this study was obtained from the University of Papua New Guinea, School of Medicine and Health Sciences (UPNG SMHS) research and ethics committee and the appropriate authority in the PMGHBTS.

RESULTS:

A total of 120 voluntary donors (VD) and 120 family replacement donors (FRD) were randomly selected each year from record books at the PMGHBTS. Thus a total of 240 donors were selected each year. Table 1 shows the gender distribution of the donors selected. Over the five years (2010 to 2014) duration of the

study 600 VD and 600 FRD were selected. This gave a total of 1, 200 randomly selected donors. Gender distribution of the 1200 donors showed 79.7% males (956/1200) and 20.3% females (244/1200). Thus the male to female ratio was 4:1.

Table 2 shows the yearly distribution (%) of the VD and FRD infected blood donors out of the 120 selected in each group. The yearly distribution shows similar trends for the VD and FRD, with no statistically significant difference between the two groups of donors. The cumulative data for the five years duration of the study indicates that out of the 1200 donors 22.9% (275/1200) were infected and 77.1% (925/1200) were not. The total number of infected donors over the five years duration of the study was slightly higher among the FRD (23.7%; 142/600) compared to the VD (22.2%; 133/600). The difference was not statistically significant. Thus, no significant difference was obtained between the two groups of donors throughout the 5 years study period.

Distribution of all the blood donors according to age groups is presented in Table 3. The highest number of donors (334/1200, 27.8%) was in the ≥35 year's age group closely followed by donors (326/1200, 27.2%) in the 20 to 24 years age group. The distribution of VD and FRD according to age groups and the distribution of infections according to age groups is also presented in Table 3. Although HIV was almost 20.0% in the 25-29 years age group, the prevalence of HBV (0.5%) was lower compared to the other age group.

Of the 275 infected donors 84.0% (231/275) were males and 16.0% (44/275) were females. The 231 male infected donors consisted of 51.5% (119/231) VD and 48.5% (112/231) FRD. The 43 female infected donors were made up of 31.8% (14/44) VD and 68.2% (30/44) FRD. Further stratification of the 275 infected donors indicated that 44.7% (123/275) were old blood donors and 55.3% (152/275) were new donors. Among the old donors 54.5% (67/123) were VD and 45.5% (56/123) were FRD. For the new donors, 43.4% (66/152) were VD and 56.6% (86/152) were FRD. Analysis of the social status of the 275 infected donors showed that 71.3% (196/275) were employed, 5.4% (15/275) were unemployed and 23.3% (64/275) were students. Among the employed donors 39.8% (78/196) were VD and 60.2% (118/196) were FRD. All the unemployed donors were FRD. For the students donors 87.5% (56/64) were VD and 12.5% (8/64) were FRD.

Single and Co-infections:

Of the 275 infected donors, 20 (7.3%) had dual infection but no triple infection. The majority of those co-infected were FRD (13/20, 65%), while 7/20 (35%) were VD. Of the 20 with dual infection, 14/20 (70%) were co-infected with HIV and syphilis, while a total of 6/20 (30%) donors were infected with HBV-syphilis. There was a statistically significant difference

between the two donor populations in HBV-Syphilis infection, while the difference in HIV-Syphilis dual infection was not (Table 4). A significant (p<0.05) difference in infection by the HBV virus between VD and FRD was demonstrated. Over the five year duration of our study more (17/600; 2.8%) FRD were infected with HBV than VD. While there was higher numbers of infections by HIV and Syphilis in both groups of donors, there was no significant (p>0.05) difference in the frequencies between them (Table 4).

VD were less likely to be infected with HBV than FRD and were also less likely (OR = 0.9) to be infected with syphilis. While the VDs are less likely to be infected with the latter two pathogens, they are more likely to be infected with HIV (Table 5).

Table 1: Gender distribution of the donors selected each year

Year	Total donors	Male donors	Female donors
2010	240	182 (75.8%)	58 (24.2%)
2011	240	181 (75.4%)	59 (24.6%)
2012	240	180 (75.0%)	60 (25.0%)
2013	240	202 (84.2%)	30 (15.8%)
2014	240	211 (87.9%)	29 (12.1%)
Total	1200	956 (79.7%)	244 (20.3%)

Table 2: Yearly distribution (%) of Voluntary and Family Replacement infected blood donors

Year	Voluntary donors (VD)	Family replacement donors (FRD)
2010	30/120 (25.0%)	30/120 (25.0%)
2011	21/120 (17.5%)	25/120 (20.8%)
2012	24/120 (20.0%)	29/120 (24.2%)
2013	26/120 (21.7%)	25/120 (20.8%)
2014	32/120 (26.7%)	33/120 (27.5%)
2010-2014	133/600 (22.2%)	142/600 (23.7%)

Table 3: Distribution of blood donors according to age groups

Age groups	≤19 yrs	20 – 24yrs	25 - 29yrs	30-34 yrs	≥35yrs
Voluntary Donors (n = 600)	114 (19%)	134 (22.3%)	75 (12.5%)	46 (7.7%)	98 (16.3%)
Family Replacement donors (n = 600)	33 (5.5%)	115 (19.2%)	70 (11.7%)	82 (13.7%)	158 (26.3%)
Total (n = 1200)	184 (15.3%)	326 (27.2%)	202 (16.8%)	154 (12.8%)	334 (27.8%)
HBV positive	0 (0%)	6 (1.8%)	1 (0.5%)	3 (2.0%)	7 (2.1%)
HIV positive	18 (9.8%)	36 (11%)	36 (17.8%)	14 (9.10%)	36 (10.8%)
Syphilis positive	19 (10.3%)	35 (10.7%)	20 (9.9%)	9 (5.8%)	35 (10.5%)
Total positive	37 (20.1%)	77 (23.6%)	57 (28.2%)	26 (16.9%)	78 (23.4%)

Table 4: The prevalence of infection between Voluntary and Family replacement donors over the five years duration of the study

	Voluntary Donors (n = 600)	Family Replacement (n = 600)	Chi square	P-value
Infection				
Infected	133 (22.2%)	142 (23.7%)	0.382	0.537
Not Infected	467 (77.2%)	458 (77.0%)		
HBV				
Positive	0 (0%)	17 (2.8%)	17.244	0.00
Negative	600 (100%)	583 (97.2%)		
HIV				
Positive	78 (13%)	62 (10.3%)	2.07	0.15
Negative	522 (87%)	538 (89.7%)		
Syphilis				
Positive	55 (10.8%)	63 (12.2%)	0.602	0.438
Negative	545 (89.2%)	537 (87.8%)		
Co-infection				
Positive	10 (1.7%)	10 (1.7%)	0.000	1.000
Negative	590 (98.3%)	590 (98.3%)		
HBV / Syphilis				
Positive	0 (0%)	6 (1%)	6.03	0.014
Negative	600 (100%)	594 (99%)		
HIV / Syphilis				
Positive	10 (1.7%)	4 (0.7%)	2.602	0.107
Negative	590 (99%)	596 (99.3%)		

Table 5: The association of infection between each donor population

	OR	95% CI
HBV	0	0
HIV	1.1579	0.8125 - 1.6502
SYPHILIS	0.8636	0.606 - 1.2307

DISCUSSION:

The result indicated that there was no statistically significant difference (p = 0.537) between the infected family replacement blood donors (FRD) and the infected voluntary blood donors (VD), 23.7% and 22.2% respectively, that participated in the present study. This finding is different from the results obtained in a study done in Laquintinie hospital in Doula, Cameron in 2014 [8] that revealed 14.3% of those infected were FRDs and 8.3% were VDs, which was similar to the results obtained in Pakistan in 2006 [15]. Two studies in Egypt also revealed higher infection among the FRD compared to the VD, which was 8.0% compared to 4.5% respectively in 2013 [16], and also 6.8% compared to 4.2% respectively in 2014 [17]. The differences in the prevalence of infections between the two groups in these studies were significant different. These results could be explained by the fact that there were more FRD than VD in the two studies. In addition, a different method of selection of donation types may have been used compared to the method used in the setting of our present study.

In developing countries like PNG, family members are more likely to willingly come forward to donate blood, especially when a family member or relative is in dire need of blood for fear of the relative dying, and also because of strong family ties. Since our study was retrospective, it is possible that some of the FRD could be friends that are not genetically related to the recipients but felt obliged to give blood out of generosity to the friend.

Our findings also indicated that VD was more frequently infected with HIV than FRD while FRD were frequently infected with syphilis and HBV (Fig 4). Differences in infection between the two donor populations were not statistically significant. There was however, a significant difference in infection with the Hepatitis B virus existed between the two donor groups (p=0.000) with FRD being the only donor population showing HBV infection than VD (2.8% and 0% respectively).

When stratified by age, a significant (p= <0.000) difference was demonstrated among the different age groups with those in the age 35 years and above were mostly infected than the younger donors (Table 3). In contrast to our

present study, a study in Nigeria in 2015 revealed no significant difference in HBV infection among the donor populations when stratified by age [18]. Our finding was however similar to other studies [16-21] that revealed significantly higher prevalence of HBV infection in FRD; although according to the authors downward trending in infection rate was observed over the years [15,17-19]. The authors also reported that despite the decreasing trend, one of the major reasons for discarding of donated blood was still due to HBV infections [25].

In a study done in Brazil in 2005 [26], the prevalence of HIV in VD was higher than FRD (19.6% and 16.1% respectively) though the difference was not statistically significant. This finding was closely related to our present study, although in Tamil Nadu the number of HIV infected donors was significantly high among the FRD [19]. High sexual activity amongst the young in Brazil was the main attribution to demonstration of significant difference between the two donor populations [26]. It is possible that the same attribute can also be a reason for the high number of HIV infection among the VD compared to the FRD in our setting. However, further studies are needed to substantiate this presumption. When stratified by age, however, a significant difference (p=<0.000) in HIV infection existed among the different age groups with those aged between 25-29 years having the highest prevalence (Table 3). In the Egyptian study in 2013 [16], HIV infection among the VD and FRD were demonstrated to be equal (0.7% and 0.7% respectively) with increasing trend observed in both, in contrast to a decreasing pattern of HIV seropositive donors in India [17, 27]. This has been partly attributed to both religious and cultural behaviour in these parts of the world where premarital sexuality is discouraged and circumcision is a common practice [16, 27]. Voluntary non-remunerated blood donation (VNRBD) has also been assumed to be one of the major reasons for such decreases [22].

In contrast to yet another Egyptian study [17], syphilis infection among the two donor populations in our present study was not statistically significant; Egyptian study: 0.3% FRD and 0% VD, p=0.024 and in our present study: 12.2% FRD and 10.8% VD, p=0.438.

This may be explained by the low number of donors (1200) used in our present study compared to the Egyptian study (17118).

In our present study no statistically significant differences were observed when the prevalence of co-infections among the donor groups was compared.

However, when stratified according to type of infections, a significant difference existed between HBV/Syphilis co-infected donors.

HBV/Syphilis co-infection was prevalent (1.0%) among the FRD. This is similar to Kumar *et al*. [28] whose study revealed HBV/Syphilis co-infections (3.7%) as more common and prevalent among FRD. HIV/Syphilis co-infection was also prevalent in this same study at 2.9%

[28], though in our study, HIV/syphilis co-infection was not found to be significant (Table 4). Furthermore, in our study, syphilis infection was mostly found among 20-24 years age group and also among those in 30 years and above age groups; while HIV infection was mostly found among the younger population 19-34 years. HBV infection was more prevalent among the older population age group above 35 years. This may indicate that sexual transmission is one of the main modes of transmission. Because of common modes of transmission, prevalence of co-infections can be detected simultaneously in the same donor group [29].

In syphilitic infections, ulceration of the genital increases the risk of transmission of HBV and also other viral pathogens such as HIV and HCV. According to Kumar et al. [28], in the presence of syphilis, HIV viral load increases, while CD4 T-cells declines. This resolves, however, when the syphilitic infection is treated. Co-infections may affect several factors during the course of treatment of one of the infections. Such factors include; clinical presentation, response to treatment and additional infection [30]. This calls for introduction of thorough donor screening methods to increase blood safety to recipients in the setting of our present study. Our results show that among the male donors infection was more prevalent among the VD (51.5%), while among the female infection was more prevalent among the FRD (68.2%). This is in contrast to Shoba & Babu [25], whose study demonstrated the male VD population having lower rates of infections (n=4538, 97.3%) than FRD (n=1426, 99.6%). On the other hand, in this same study, the female VD population had higher rates of infection (n=124, 2.7%) than FRD (n=6, 0.4%) [25]. This is in contrast to the current study where the number of infected female FRD was two times higher than the female VD (n=30, 68.2% vs n=14, 31.8%) respectively.

The differences in the data presented may be due to several reasons. More male VD coming forward to voluntarily donate than females who would rather give to family and friends than to someone else they do not know. Apart from this, females are more likely to be the ones visiting sick relatives quite often in hospitals than males, and therefore, are on hand for when there is urgent need for replacement donations. These females quite often do not consider their social status before donating. These assumptions however need to be substantiated through large prospective studies in our setting.

Among the donors that have been donating or have donated once or more in the past (old donors), infection was more prevalent among the VD (54.5%) compared to the FRD (45.5%), while among the donor population that donated for the first time (new donors), infection was more prevalent among the FRD (56.6%) compared to the VD (43.4%). Difference among the two groups of donors was not statistically significant (p=0.076). According to Jemia &

Gouider [21], infections were significantly higher for HBV and syphilis in older (30-39 years old) first time replacement donors than first time voluntary, while HIV infection rates were insignificant. This is in concordance with this study except that, in this study, there was no significant difference in infection rates between the two groups. The risk of infection is usually higher in new FRD because they may have been pressured or may have been paid [15] to donate and therefore may have concealed their risky behaviour, escaping being excluded during the pre-donation screening process. In the case of new VD, they may simply be donating for the sole purpose of knowing their serological status and therefore feel safe to donate.

In this study, more old VD were infected than FRD. This is in contrast to other studies [31-32], where the prevalence rates of infection was low among the old VD. Further studies are suggested to determine the reasons for such a scenario in our setting. It is possible that the screening process is not very effective. According to Jemia & Gouider [21] and Marantidou *et al*. [33], FRD increases the risk of HBV infection transmission. In a review on VNRBD, sound evidence have supported the notion that new VD may not be safer in donating blood than FRD and that only old VD increases blood safety [34]. The findings of this article implied that if VNRBD is the only source of blood to improve safety, then there will be a lot of deferrals that will lead to chronic shortage of blood supply, also taking into consideration the cost in keeping patients in hospitals, while waiting for VD to donate. In PNG, where blood banks continue to face blood shortages [12], we cannot afford to completely do away with FDR. In fact, both types of donations should be encouraged.

Infections among employed FRD was significantly higher than among students and unemployed donors (p<0.000). According to some authors [22, 25] professional donations should be discouraged; individuals should be encouraged to become voluntary blood donors, though such professional donors can still continue to donate in the guise of friends or relatives. According to the authors, the banning of professional donors resulted in reduction in discards of infected donors' blood [22]. Despite this reduction, donated blood may still be discarded due to other reasons such as contamination by bacteria through culture, clotting, haemolysis or expire blood [25].

Targeting students for voluntary blood donation could be a better way to reduce transmission of pathogens through transfusion. However, knowledge and attitudes on blood donation is of paramount importance. A study among Health Science Students in an Indian university reported that the majority of the students indicated that if only they are more knowledgeable about the importance of donating blood, they will be willing to donate [35]. Among Health care support staff in an Indian Tertiary Care Hospital, knowledge about

blood donation regarding safety and eligibility was lacking. Furthermore, ways in which they can be motivated to donate blood was also low [36]. These are indications that awareness & motivational campaigns should be promoted to bring about positive attitudes towards blood donation and hence increase blood safety. Students are young, healthy and vibrant. In fact, the WHO is promoting a younger generation of voluntary donors, in collaboration with other stakeholders to live healthy life style that would contribute to safe blood donation [37]. In the present study, the likelihood of voluntary donors being infected with HBV is very low, unlike with syphilis and HIV. Infact, the likelihood of a VD being infected with HIV is high. This finding supports the findings of Jemia & Gouider [21] whose study demonstrated that replacement type of donation apart from the male gender and age are independent risk factors for HBsAg carriage. However, in his review on evidence on the pros and cons of VNRD-only strategy, Allain, [34] observed that in two African countries, significantly high HBsAg prevalence existed in first time VNRD than replacement donors. This indicated the need to carefully categorize the donor populations into clearly defined and distinct groups other than generalizing. The high probability of VD being infected with HIV in this study may mean that many of these donors may have been first time VD and not necessarily repeat donors (old donors), who donate regularly and know their serological status. This hypothesis needs proving through prospective studies in this setting.

CONCLUSION:

This study revealed statistically insignificant differences between VD and FRD except HBV infection. However, the likely hood of VD being infected with HIV is high; therefore FRD should not be discouraged from donating blood, especially in settings that face acute shortages of blood supply.

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