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Human Pegi Virus (HPgV) Incidence and Factors Associated With Its Infection among Blood Donors In Kano, Nigeria

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Abstract: Background: The severity of hepatitis HPgV and the incidence is not established clearly in Africa. Molecular estimation and analysis of phylogenic tree of nucleotides and amino acids of viruses HBV, HIV, HPGV and HCV proposed an association amide the different viruses. Though, there are a closer relationship in amino acid sequence was found among HCV and HPGV viruses, whereas, its association with other hepatitis viruses is not cleared until now. Yet its co-infection with HIV suppressed the growth and multiplication of HIV, so diminishing the development of HIV sero-positive individuals into AIDS. Conversely, HPGV as hepatotrophic virus must given an attention to be screened and studied **Objective:** The study was to establish the prevalence of HPGV, its socio-demographic risk factors and its co-infection with HBsAg, HCVAb and HIV among blood donors in Kano, Nigeria. **Methods:** A total of 400 blood donors from 3 health facilities in Kano were examined for HBsAg and HCVAb by rapid strip immuno-chromatography technique, while, HIV was examined by Nigerian algorism (UNI-GOLD and STAT PACK HIV test kits and HPgV by Ag-based ELISA technique). Socio-demographic data were collected from each participant by a closed-ended questionnaire. **Results:** The socio-demographic data revealed that 167 (41.8%), their ages ranged from 25-32years, males representing 76.2% (n=319) and females representing 20% (n=81), with 253 (63.2%) married. The level of education of participants was 40.5% 1ry level and 34.8% were traders. The incidence of hepatitis GB virus C among blood donors was 0.8%. Positive results for HPgV was (R =.071) for HBsAg, (R =0.135) for HCVAb and (R=0.299) for HIV. a A significant relationship (P =....) was found among HPGV and coexistence of HIV. The ages of positive HPGV test participants in one male and two females were ranged from 17 to 24 and from 25 to 32 years. **Conclusion:** The presence of HPgV of 3 (0.8%) among blood donors in Kano, proposed its rate at a higher percentage amide the general public in the society. The co-existence of HPGV with HIV, HBV and HCV amide the blood donors proposed its co-existence with a higher rates between the high risk groups for HCV, HIV and HBV infections. **Recommendation:** Further community-based survey, particularly among the high risk groups, is recommended to establish the prevalence and the socio-demographic factors associated with HPGV infection in the study area.

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Keywords: Human; Pegi Virus (HPgV); Factor; Infection; Blood Donor; Nigeria

Introduction:

This chapter presents the background, problem statement, purpose, objectives, and research questions, scope of study, significance and conceptual frame work.

Historical background

After the identification of hepatitis A and B viruses (HAV & HBV), there were speculations that some non-Anon-B transfusion associated viral hepatitis agents exist (Bradley *et al.,* 1983). These additional hepatotrophic viruses were later identified as HCV, HDV and HEV (Choo *et al.,* 1989). However, after these five (5) viruses had been described, additional cases of hepatitis that apparently were caused by hepatotrophic viruses (sometimes called non-A, non-E viruses) were still occurring **(Rowen, 2012).** Another investigation by Dawson *et al;* (1995) and Zuckerman *et al;* (1996) led to the independent discovery of HGV2 and GBV-C. A novel agent called hepatitis F virus was identified by some investigators as a novel virus, transmitted via GIT, but this observation has not been confirmed and was likely a premature designation (Heringlake *et al.,* 1996).

Nowadays, GBV-A beside GBV-C, and (GBV-D), were suggested to make a 4th genus inside the Flaviviridae called 'Pegivirus' for 'tenacious G virus' and GBV-C was recommended to be retitled as 'human Pegivirus' or HPgV (Stapleton, 2011). HPgV is not presently allocated to any of the three Flaviviridae genera (flavi, pesti and hepaci).

HPgV is categorized as a member of Flaviviridae family depend on its sequence of nucleotides and genome group, and is thoroughly correlated to human virus HCV (Mohr and Stapleton, 2009). Dissimilar to HCV, GBV-C seems to be lymphotropic, and the virus is formed *in vitro* by B and T lymphocytes obtained from HPgV infected subjects (George *et al.;* 2006). Primary researches recorded the presence of HPgVRNA in hepatic samples, reliable with it being a hepatitis virus (HGV). Conversely, consequent investigations established that the comparative quantity of HPgV RNA in blood versus liver was high, postulating that the hepatic tissues may not be the place of repetition (Mohr and Stapleton, 2009). Moreover, single strand HPgVRNA, was a pointer of viral transcription inside cells, and it was observed in spleen and bone marrow samples proposing a hematopoietic site of multiplication. These outcomes increase the probability that lymphocyte progenitor cells may form the primary permissive cell for HPgV multiplication.

The first clinical illness of human pegi virus (HPgV) was observed in 1966, in a 34-year-old surgeon named G. B (initials) who had acute hepatitis of moderate enzymatic activity. It was from his serum that GB hepatitis (currently called HPgV) agent was first isolated (and named using his initials as GB).). On the third day, his serum was serially passed into an experimental animal, Sanguineous SP [a tamarin], for further investigation of the virus (Dawson *et al.,* 1995). Representational difference analysis was used to clone the nucleotide sequences from the serum of the infected tamarin.

Investigators at Abbott Laboratories discovered two flavivirus-like genomes which were called GBV-A and GBV-B (Dawson *et al.,* 1995). It was later determined that GBV-A and GBV-B were most likely nonhuman viruses that only infect tamarins (Dawson *et al.,* 1995).

HPgV (human Pegivirus) was previously identified by two different groups of researchers in the study of hepatitis non-A, non-B, non-E cases (Buijk *et al.,* 1995). HPgV is a lymphotropic human virus that is connected with HCV virus(Alter *et al.,* 1996). In 1995 in West African, Abbott Laboratories recorded a novel human virus in the blood serum of a patient characterized by a non-(A–E) hepatitis which they called HPgV based on nucleotide sequence. Its nucleotide sequence were similar to those of two initial viruses named GBV-A and GBV-B viruses (Simons *et al.,* 1995). GBV-A and B were identified in tamarins that induced hepatitis after inoculation with a surgeon`s serum whose marks were G.B. (Leary *et al.,* 1996).

Theoretical background:

Flaviviridae family are including mainly GBV-B, HCV, GBV-A, GBV-D and HPgV. Matching the genomes of HPGV with that of GBV-A, GBV-B, and HGV demonstrated less than 32% similarities of their RNA. This proved HPgV virus genome to be an independent genome (Robertson, 2001). The genome of HPgV virus is a positive-sense RNA that similar in the sequence and organizational to some viruses within the family of Flaviviridae (Linnen *et al.,* 1996). The original HPgV isolate contains a continuous open reading frame (ORF) preceded by a 5' untranslated sequence of 458 nucleotides and followed by a 3' untranslated region (UTR) of 315 nucleotides (Barbara *et al.,* 1999). The ORF encodes a polyproteins of 2873 amino acids with a number of characteristic motifs: two chymotrypsin-like protease motifs, an RNA-dependent RNA polymerase motif and a helicase motif. The HPgV genomic organization is similar to other members of the Flaviviridae, with the recognized structural genes located at the 5'-end of the genome followed by supposed nonstructural genes. The 5' UTRs are highly conserved (Hofacker *et al.,* 2012). The HPgV is 9125 nucleotides in length, with a continuous ORF encoding a poly-protein of 2906 amino acids. The ORF is preceded by 343 nucleotides and followed by an additional 61nucleotides of presumably un-translated sequence (Chalmers *et al.,* 1996).

HPgV, the molecular weight about 9.3 kb, a single stranded positive RNA genome of and includes a single open reading frame (ORF) encoding five non-structural (NS2, NS3, NS4, NS5A, and NS5B) and two structural (E1 and E2) proteins. HPgV does not seem to encode a C (core or nucleocapsid) protein like, for example, hepatitis C virus. However viral particles have been reported to have a nucleocapsid of which origin remains unknown (Stapleton *et al.,* 2010).

Conceptual background

The role of HPgV (formerly known as GBV-C/HGV) in co-infection with other hepatitis viruses is not clearly understood, particularly in its response to antiviral therapy and its impacts on liver transplantation (Di Bisceglie *et al.,* 1999.). HPgV is a blood-borne transmissible viral element that often found as a co-infection with other hepatitis viruses and HIV due to similarity in the modes of transfer. The incidence of HPgV among blood donors reached about 0.9 -10% all over the global, in developed countries it is found to be 1–5% among healthy blood donors

while in developing countries, it is up to 20% among blood donors (Mohr and Stapleton, 2009) and in the United States it reached 1.7% among blood donors (Mikhailov, 1997).

Most of patients infected with HPgV through blood transfusion centers do not progressed to induce chronic hepatitis, although human Pegi virus viremia often continues without a remarkable indications by biochemical parameters for induction of hepatitis. HGV RNA in the serum has been present in 0-50% of individuals with fulminant hepatitis of indefinite cause and 14-36% of individuals with cryptogenic cirrhosis (Jack and Nirjal, 2012). The association between HPgV and chronic non-A-E hepatitis in causing acute and chronic liver diseases remains uncertain (Cheung *et al.,* 1997).

HPgV infection has not been proved to be connected with any disorders, but, Jack and Nirjal (2012) showed a link among continued HPgV infection and enhanced survival in HIV-positive subjects. Infection with HPgV modestly suppress in vivo T cell homeostasis via many postulations, such as: modulation of receptor expression and diminution of T cell activation, cytokine release, chemokine, apoptosis and proliferation. Other investigators tried to explain the previous observations and proposed many mechanisms comprising modification of antiviral cytokine release, Fas-mediated apoptosis, direct inhibition of HIV-1 entry, HIV co-receptor expression and T-cell activation. (George, 2006). These mechanisms were thought to be possible contributors to improvement of HIV clinical outcomes (Yirrell *et al.,* 2007*)*. These clinical observations was confirmed in vitro and prove an anti-HIV replication impact of HPgV(Jack and Nirjal, 2012). Because HPgV primarily recites and replicates in lymphocytes (CD4 and CD8) and not in hepatocells, this could explain why it inhibits HIV and could not cause hepatitis respectively (Stapleton, 2011). Additional understanding of these modes of action may open new strategies for HIV/AIDS treatment.

Contextual background

Viral hepatitis is a major problem worldwide and is caused by five well-characterized etiologic agents. These are hepatitis viruses A, B, C, D, and Ewhich are distinct viruses whose molecular structure and disease associations are well known(Carrat *et al.,* 2008).All the five viruses can cause acute hepatitis, but only hepatitis B, C and D can result in chronic infection. With the advent of precise serological and virological testing for all five viruses, it was recognized that 5 to 15% of patients with acute or chronic viral hepatitis were negative for all viral markers and had an illness operationally termed non-A-E hepatitis(Bowden*et al.,* 1996).

HPgV infection has been distributed all over the world and presently infects nearly 1/6 of the world's inhabitants. High incidence is recorded between individuals with the risk of blood and blood product exposures and parenteral transmission, those on intravenous drug users and hemodialysis (WHO, 2000). Vertical transmission and sexual contact of HPgV may happen. Approximately 14–36% of drug users and 10–25% of hepatitis C infected individuals who are seropositive for HIV-1 demonstrate the presence of HPgV infection (Carolynne *et al.;* 2012). Another virus, the GB virus C (or HGV), which appears to be the same virus as HPgV, has been identified, confirmed, and cloned(Heringlake *et al.,* 1996). Two recent reviews on HGV4'5 offered limited information on the clinical relevance of HGV in various diseases(Heringlake *et al.,* 1996).

The transmission route of HPgV via blood and blood product is similar to that of other hepatitis viruses and HIV, while both HIV and other viral hepatitis can cause acute or chronic illness HPgV is not related to illness as reported by Jack and Nirjal, (2012), however its co-infection with HIV slows down HIV replication therefore reducing morbidity and mortality of HIV (AIDS).

The aim of the study

The target from this investigation was to estimates the frequency of human pegi virus and factors linked with its infection between blood donors in Kano, Nigeria.

Methodology

Study Design

The work was a cross-sectional descriptive quantitative analysis using closed ended structured questionnaires and laboratory blood tests. It was a hospital based study comprising of three (3) facilities namely AKTH, MMSH and MAWSH from where the study participants were recruited.

Study area

The study was conducted in 3 tertiary health institutions of Kano city a North-Western state, Nigeria. The hospitals were Aminu Kano Teaching Hospital (AKTH), Murtala Muhammad Specialist Hospital (MMSH) and Muhammad Abdullahi Wase Specialist Hospital (MAWSH).

Study participants

The participants were blood donors from the three tertiary hospitals in Kano city.

Sample Size determination

The research sample size will be determined by using the Slovin's (1960) formula: n =

$N \div 1 + Ne^2$, where it is defined as follows:-

n = Sample size

N = Target population

e^2 = Margin error $(0.05)^2 = 0.0025$

➢ Total blood donors population in the three hospitals (Total population) = **13,415**

Therefore n (sample size) = 13,415 ÷ 1 + (13,415) x 0.0025 = **388.418**

The sample size was extrapolated to 400, because data and samples were already collected up to that. New Sample Size = 400.

Sampling techniques

A consecutive sampling technique was used to obtain the study samples in which 5ml blood was collected using vacutainer-set from all blood donors that suit the set inclusion/exclusion criteria were recruited for the study.

Data analysis

The data was analyzed using univariate, bivariate and multivariate (co-relation studies) statistical analysis by use of measure of dispersion and location, at 95% (0.005%) level of confidence.

Ethical Consideration

The study was conducted after obtaining ethical clearances from MUST IREC, AKTH and HMB Kano ethical review committees. All participants consented by signing consent form (Appendix II) after the merit and demerit had been explained to them. Their details were kept confidential. The samples taken were used for the study only.

Results

The demographic characteristics of the study participants

Out of the 400 participants, 318 (79.5%) were males, and 82 (20.5%) were females. The age of participants ranged from 17–72 years with majority 167 (41.8%) in the age bracket of 25-32. Two hundred and fifty three (63.3%) were married, 138 (34.5%), were single, 7 (1.8%) were widowed and 2 (0.5%) divorced/separated. Educational status of the participants showed that 162 (40.5%) had primary education, 136 (34.0%) had post-secondary school and only 41 (10.3%) had no formal education. Majority of the participants were small scale traders 139 (34.8%), public servants were 76 (19.0%), artisans were 52 (13.0%), unemployed were 50 (12.5%), students 48 (12.0%), drivers 18(4.5%) and farmers 17 (4.3%) (Figure 8).

Figures 4-9: Socio-demographic Background characteristics of the respondents

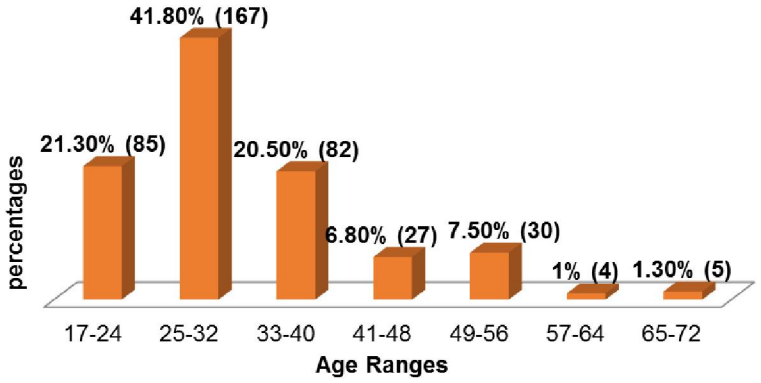

Figure 1: Age Frequency
Source: primary data

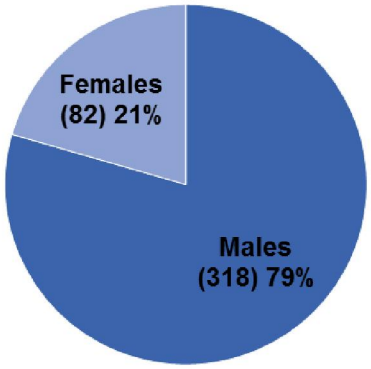

Figure 2: Gender
Source: primary data

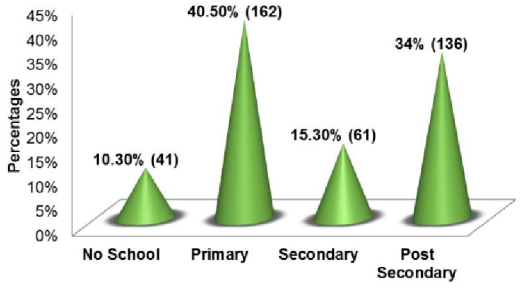

Figure 3: Level of Education
Source: primary data

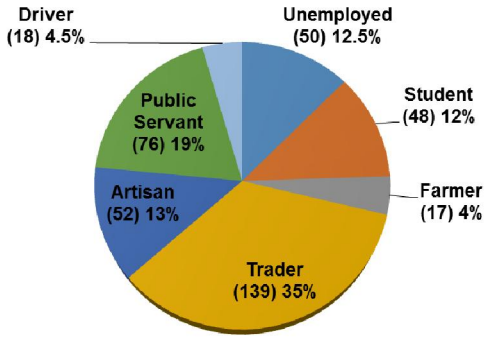

Figure 4: Occupation
Source: primary data

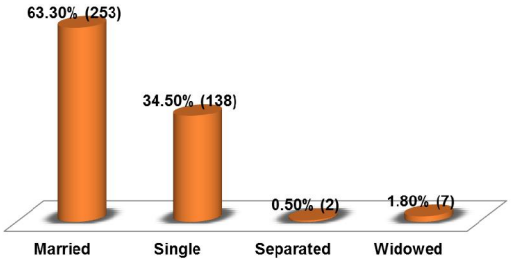

Figure 5: Marital Status
Source: *Primary Data*

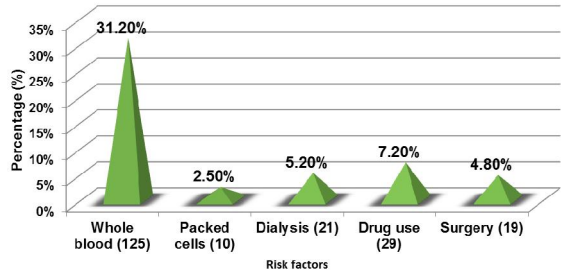

Figure 6: positivity rates of HPgV, HCV, HBC and HIV among 400 blood donors
Source: primary data

The history of parenteral risk factors among participants showed that 125 (31.2%) had whole blood transfusion, 10 (2.5%) had packed cells transfusion, 21 (5.2%) had dialysis, 29 (7.2%) had parenteral drug use while 19 (4.8%)

Figure 10 shows the positivity rates of HPgV, HCV, HBC and HIV among 400 blood donors. Sixty six (66) participants (16.5%) had tested for at least one of the four viruses, with 37 (9.2%) infected with HBV, 14 (3.5%) infected with HCV, 12 (3.0%) infected with HIV and only 3 (0.8%) infected with HPgV. The prevalence of HPgV among the participants is therefore 0.8%.

4.2HPgV co-infections with HBV, HCV and HIV

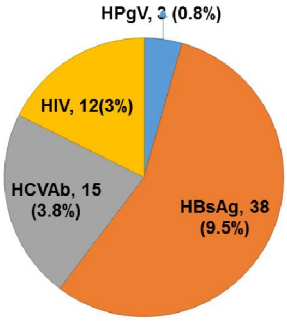

Figure 9: History of parental risk factors for HPgV, HBV, HCV and HIV infetions among participants
Source: primary data

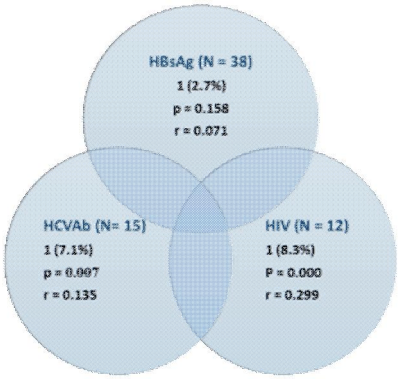

Figure 7: Frequency of HPgV co-infection with HBV, HCV and HIV blood donors (N=68)
Source: primary data

Figure 11 shows the prevalence rate of HPgV infection among 66 blood donors who had HBV, HCV and HIV infections. Results showed that 3 (4.5%) of HPgV positive donors had 1 co-infection each with HIV (8.3%, p =.000, r = 0.299), HCV (7.1%, p=0.007, r = 0.135) and HBV (2.7%, p = 0.158, r = 0.071) respectively. There was as statistically significant correlation between the co-infection of HPgV with HIV and HCV, but not with HBV.

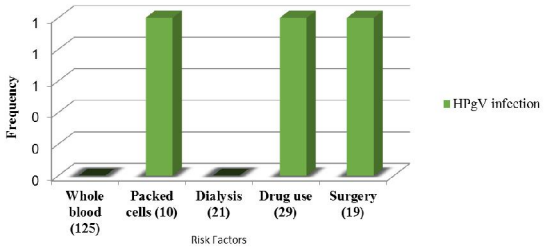

Figure 8: Frequency of HPgV infection in to the parenteral risk factors for infection
Source: primary data

The occurrence of HPgV among participants indicated that HPgV infection existed among 1 participant each, with history of packed cells transfusion (0.1%, p = 0.002), drug use (3.5%, p = 0.028) and surgery (5.3%, p =0.028).

4.3 The socio-demographic risk factors on single and co-infection of HPgV

The third objective of the study was to determine the effect of socio-demographic risk factors on both single and co-infection of HPgV. This section provides socio-demographic characteristics which included; age, gender, marital status, level of education, and occupational status of the participants in relation to HPgV, HBV, HCV and HIV positive blood donors in Kano State, Nigeria (Figure 10 - 14).

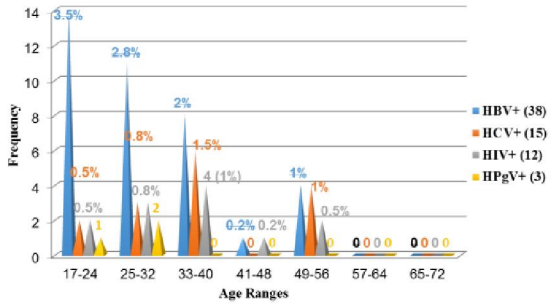

Figure 9: HPgV co-infection with HBV, HCV and HIV in relation to ages of the participants
Source: primary data

Infection with all the 4 viruses occurred among the age groups of 17-56 years among the participants. Infection with HBV occurred among 14 (3.5%) of the participants with the age bracket of 17-24 years. Six (6) participants each had infection with HCV (1.5%) and HIV (1.2%) among the age group of 33-40 years. Infection with HPgV occurred participants of among 2 (2.4%) of age groups of 25-32 years and 1 (1.2%) among the age bracket of 17-24 years.

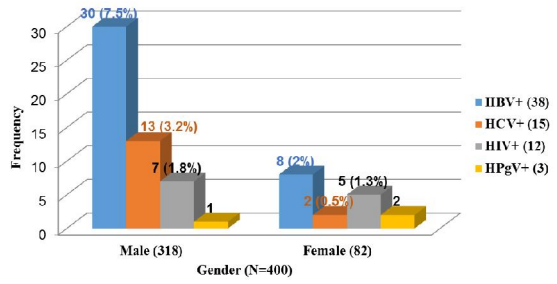

Figure 10: HPgV co-infection with HBV, HCV and HIV in relation to Gender
Source: primary data

More males were infected with HIV 8 (1.9%), HBV 36 (7.5%) and HCV 13 (3.2%) than females infected with HIV 7 (1.75%), HBV 8 (2.0%) and HCV 2 (0.5%). However, 1 (0.25%) male and 2 (0.5%) females were infected with GBV-C (p = 0.015)

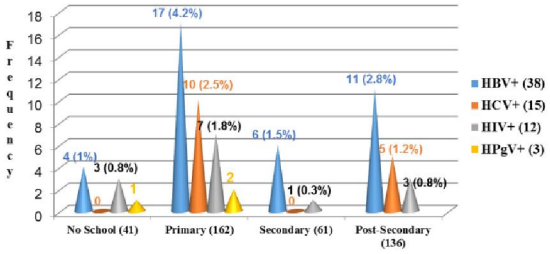

Figure 11: HPgV co-infection with HBV, HCV and HIV in relation to level of education
Source: primary data

Participants with at least primary level of education constituted the higher proportion of infections with HIV 8 (1.2%), HBV 17 (4.2%), and HCV 10 (2.5%) than the rest of the educational groups (p = 0.312) which is not statistically significant.

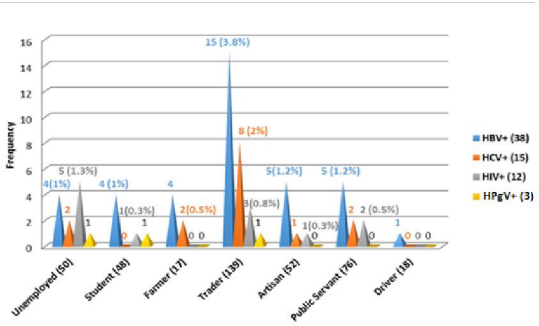

Figure 12: HPgV co-infection with HBV, HCV and HIV in relation to occupation
Source: primary data

Results showed that Traders constituting 139 (34.8%) had higher proportion of participants infected with HIV 4 (0.8%), HBV 15 (3.8%), HCV 8 (2.0%) and HPgV1 (0.2%). The lowest proportion were found among Artisans infected with HIV 1 (0.2%), HBV 5 (1.2%), HCV 1 (0.2%) and none having HPgV infection.

Results showed the existence of the 4 viruses in only married and single participants. Married participants had higher infection rate with HIV 9 (2.2%), HBV 20 (5.0%), HCV 10 (2.5%) than participants who were Single with HIV 5 (1.2%), HBV 18 (4.5%), and HCV 5 (1.2%). However, the 3 participants with HPgV infection comprised 2 (0.5%) singles and 1 (0.25%) married.

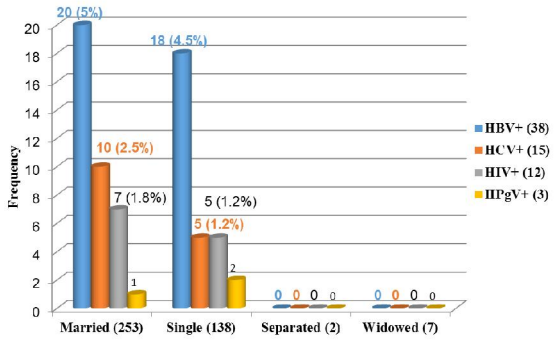

Figure 13: HPgV co-infection with HBV, HCV and HIV in relation marital status
Source: primary data

Discussion

The prevalence rate of HPGV infection level

In this study blood donors were used to determine the prevalence of HPgV in the study area because they represent a proportion of apparently healthy individuals in the community. Furthermore blood donors could be potential sources of parenteral transmission of HPgV to the recipients (Collingham *et al.,* 1997)). Other workers have reported the prevalence of HPgV among blood donors (Novikov, 2000). In this study, the prevalence rate of Hepatitis HPgV among blood donors in the study area was 3 (0.8%). This finding is relatively lower than the previous findings of 1.7% reported by Ampurdanes *et al*., (1998), 2% in North Vietnam Nguyen *et al* (2002) and 3% in Uganda as reported by Yirrell *et al.,* (2007). Lower prevalence of HPGV in this study compared with the previous studies could be due the larger number of participants () than the 400 participants in this study.

The frequency of HPGV co-infections with HBV, HCV and HIV

Phylogenic tree and Molecular analysis of nucleotides and sequences of amino acids of HBV, HCV, HIV and HPgV proposed an associations among the viruses. On the other hand, closer amino acid sequence connection found amide HCV and HPgV ((Linnen *et al*., 1996; clustal W2, 2015). In this study, 66 participants (16.5%) among the 400 blood donors tested positive for at least one of the four viruses, with 37 (9.2%) infected with HBV, 14 (3.5%) infected with HCV, 12 (3.0%) infected with HIV and only 3 (0.8%) infected with HPgV. The prevalence of HPgV alone among the participants was therefore 0.8%.

The prevalence rate of HPgV co-infection among 66 blood donors who had HBV, HCV and HIV infections was 3 (4.5%). Individuals with positive tests for HPgV tested positive for HBsAg (R =.071), HCVAb (R =0.135) and HIV (R=0.299) respectively. The co-infection rate of 4.5% obtained in this study is lower than the 10% co-infection of HPGV with HBV and the 11% co-infection with HCV reported by Barusruk, (2006). Yirrell *et al.,* (2007) reported that HPgV viremia in HIV has been associated with an improved prognosis in HIV- 1-co-infected individuals in Uganda. The lower value obtained in this study could be due to the relatively lower sample size of 400 participants compared to the 13,610 used by Barusruk (2006). Furthermore the higher sensitivity of the molecular techniques used in that compared with the phenotypic method used in this study could explain the difference.

The socio-demographic risk factors on single and co-infection of HPGV

Findings of this study suggest that more males than females donated blood for transfusion in the study area. The socio-demographic characteristics of the participants indicated that infection with all the 4 viruses occurred among the age groups of 17-56 years among the participants. Infection with HPgV occurred participants of among 2 (2.4%) of age groups of 25-32 years and 1 (1.2%) among the age bracket of 17-24 years, with more females having HPgV infection than males.

Some socio economic characteristics such as levels of education, occupation and marital status of the participants showed some regular trends in the existence and co-infections of HPgV with HBV, HCV and HIV. However, available data from this study does not allow for the correlation analyses between the existence of HPgV, its co-infection with other viruses and the socio-demographic characteristics. For instance, infection with HPgV and its co-infection with other viruses were found to be higher among participants with at least primary level of education than other educational groups and among the traders and the married participants. The limited samples that tested positive for HPgV (3) in this study does not allow for statistical correlation analysis of these characteristics with the prevalence of HPgV and its co-infection with other viruses.

Conclusion

The prevalence of HPgV among blood donors in Kano, Nigeria was 3 (0.8%). The occurrence of these viruses among blood donors proposed its incidence at a higher rate between the population in the society. The co-existence of HPgV beside HCV, HIV and HBV amide the individuals proposes its co-existence in higher rate between the high risk groups for HCV, HIV and HBV infections.

Recommendation

Further community-based survey, particularly among the high risk groups, is recommended to establish the prevalence and the socio-demographic factors associated with HPgV infection in the study area.

References

1. Robertson, 2001. Ampurdanes *et al*., (1998)
2. Alter H, Fry KE, Krawczynski KZ, Linnen J, Wages J Jr, and Zhang-Keck ZY, (1996). Molecular cloning and disease association of hepatitis G virus: a transfusion-transmissible agent. Science; 271:505-508.
3. Barbara Tribl, Maximilian Schöniger-Hekele, Dagmar Petermann, Silvia Bakos, Edward Penner and Christian Müller (1999). Prevalence of HPGV/HGV-RNA, virus genotypes, and anti-E2 antibodies in autoimmune hepatitis HPGV/HGV in Autoimmune Hepatitis. The American Journal of Gastroenterology 94, 3336-3340 | doi:10.1111/j.1572-0241.1999.01452.
4. Bowden DS, Moaven LD, and Locarnini SA (1996). New hepatitis viruses: Are there enough letters in the alphabet? Med J Australia; 164:87-89.
5. Bradley DW, Maynard JE, Popper H, Cook EH, Ebert JW, McCaustland KA (1983). Post transfusion non-A, non-B hepatitis: physciochemical properties of two distinct agents. J Infect Dis; 148:254-265.
6. Buijk SL, Chalmers ML, Dawson GJ, Desai SM, Erker JC, Leary TP, Muerhoff AS, Pilot-Matias TJ, Schlauder GG and Simons JN, (1995). Identification of two flavivirus-like genomes in the GB hepatitis agent. Proc Natl Acad Sci USA; 92: 3401-3405.
7. Barusruk S and Urwijitaroon Y (2006). High prevalence of HGV coinfection with HBV or HCV among northeastern Thaiblood donors. Southeast Asian J Trop Med Public Health; 37: 289-293.
8. Carolynne Schwarze-Zander, Jason T Blackard and Juergen K Rockstroh (2012). Role of HPgV in modulating HIV disease. NIH Public Access.
9. Carrat F, Larrat S, and Piroth L (2008). Prevalence and impact of HPGV, SEN-V and HBV occult infections in HIV-HCV co-infected patients on HCV therapy. J Hepatol 2008; 49:892.
10. Chalmers ML, Erker JC, Leary TP, Muerhoff AS, Pilot-Matias TJ and Simons JN, (1997). Sequence and genomic organization of HPGV: a novel member of the Flaviviridae associated with human non-A-E hepatitis. J Med Virol; 48:60-67. Cheung RC, K. E. Hepatitis G virus: Is it a Hepatitis Virus?. *West Journal of Medical virology, 167*, 23-33.
11. Cheung RC, Keeffe EB, and Greenberg HB (1997) Hepatitis G virus: is it a hepatitis virus? West J Med: 167:23-33.
12. Choo Q-L, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. (1989). Isolation of a cDNA clone derived from a blood-borne non-A, non-B hepatitis genome. Science; 244:362-364.
13. Collingham K, Harrison P and Skidmore SJ (1997) High prevalence of hepatitis G virus in bone marrow transplant recipients and patients treated for acute leukaemia. Blood; 89:3853–6.
14. Dawson GJ, Erker JC, Leary TP, Muerhoff AS, Pilot-Matias TJ and Simons JN, (1995). Genomic organization of GB viruses A and B: two new members of the Flaviviridae associated with GB agent hepatitis. J Virol; 69:5621-5630.
15. Di Bisceglie AM, Fan X, Xu Y, Solomon H, Ramrakhiani S, Neuschwander-Tetri BA. (1999) Is hepatitis G/GB virus-C hepatotropic? Detection of hepatitis G/GB virus-C viral RNA in liver and serum. J Med Virol. 58:160-164.
16. *George SL, Varmaz D, and Stapleton JT (2006). "GB Virus C Replicates in Primary T and B Lymphocytes". J. Infect. Dis. 193 (3): 451–4. doi:10.1086/499435. PMID 16388494*
17. Heringlake S, Tillmann HL, and Manns MP (1996). New hepatitis viruses. J Hepatol; 25:239-247.
18. Hofacker IL, Thurner C, Witwer C and Stadler PF (2012). Conserved RNA secondary structures in Flavivirus Genomes. *Journal of General Virology, 85*(5), 1113-1124.
19. Jack T. Stapleton and Nirjal Bhattarai (2012), GB virus C: the good boy virus? Trends in Microbiology, Vol. 20, No. 3.
20. Leary T P, Muerhoff S A, Simons J N, Pilot-Matias T J, Erker J C, Chalmers M L, Schlauder G G, Dawson G J, Desai S M, and Muchshwar I K. (1996). Sequence and genomic organization of HPGV: a novel member of the flaviviridae associated with human non-A-E hepatitis. J Med Virol. 48:60–67. [PubMed]
21. Linnen J, Wages J, Jr, Zhang-Keck Z Y, Fry K E, and Krzysztof Z, (1996). *Molecular cloning and disease association of hepatitis G virus: a transfusion-transmissible agent. Science*. 271:505–508. [PubMed]
22. Mikhailov MI, (1997). Hepatitis G: Problem of Studies. *journal of viral Hepatol, 1*, 3-11.
23. Mohr EL and Stapleton JT. (2009) GB virus type C interactions with HIV: the role of envelope glycoproteins. J. Viral Hepat. 16:757–768. [PMC free article] [PubMed]

24. Nguyen MH, Keeffe EB and Cheo RX (2002). Screening for hepatocellular carcinoma. J ClinGastroenterol; 35:886-891.
25. Novikov DV (2000). Molecular biological characteristics of HCV. Abstract of dissertation for Candidate of Medical Sciences: 1-22.
26. Stapleton, J. T.; Foung, S.; Muerhoff, A. S.; Bukh, J.; Simmonds, P. (2011). "The GB viruses: A review and proposed classification of GBV-A, HPGV (HGV), and GBV-D in genus Pegivirus within the family Flaviviridae". Journal of.
27. Yirrell DL1, Wright E, Shafer LA, Campbell E, Van der Paal L, Kaleebu P, Grosskurth H, Whitworth JA (2007) Association between active GB virus-C (hepatitis G) infection and HIV-1 disease in Uganda. Int J STD AIDS. 2007 Apr;18(4):244-9.
28. WHO. (2000). A special report on liver diseases: causes, prevention and control.
29. Wiwanitkit. (2005). Hepatitis G virus RNA positivity among the voluntary blood donors: A summary. *Journal Hepatol, 4*,.43-46.
30. Zuckerman. (1996). Alphabet of Hepatitis Virus. *Lancet Journal of Virology., 347*, 558-559.

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