

## **PATTERN OF LIPID PROFILE LEVELS IN HIV SERODISCORDANT COUPLES IN JOS PLATAEU STATE, NIGERIA.**

**Type of article:** Original Research Article

### **Abstract**

This was a cross sectional study designed to determine the pattern of lipid profile levels in HIV serodiscordant couples in Jos, Nigeria. A total of 20 discordant HIV couples (40 patients) and 20 controls (40 non HIV couples) aged between 18 and 49 years were included in the study. 5ml of fasting venous blood sample was collected from each participant into plain containers for the evaluation of lipid profile. Total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), very low density lipoprotein cholesterol (VLDL-C) and low density lipoprotein cholesterol (LDL-C) were assayed using standard methods. The results showed that HIV discordant test group had significantly higher mean serum TG, VLDL-C, and LDL-C levels whereas HDL-C values were significantly lower than in the control ( $p < 0.05$ ). There was no significant difference in TC levels in groups when compared to the control ( $p > 0.05$ ). The male HIV discordant test group had higher TG and VLDL-C values ( $p = 0.001$ ;  $0.002$ ) and lower HDL-C ( $p = 0.000$ ) than in the male control group ( $p = 0.001$ ) while the female HIV discordant test group had significantly higher LDL-C and lower HDL-C levels ( $p = 0.001$ ;  $0.000$ ) than in female control group. Male HIV-exposed seronegative partners had significantly higher TG and VLDL-C with lower HDL-C levels ( $p < 0.05$ ) compared to male control while female exposed seronegatives had significantly lower HDL-C level ( $p = 0.000$ ) than in the female control. Furthermore, female HIV positives had significantly higher LDL-C and lower HDL-C levels than in the female control ( $p < 0.05$ ). This study revealed significant alterations in lipid profile levels in the HIV serodiscordant couples which warrant further studies.

**Key words:** HIV, serodiscordant couples, Lipid profile, Jos.

## Introduction

The human immunodeficiency virus (HIV) is a lentivirus (a subgroup of retrovirus) that causes HIV infection [1, 2]. Although it has been proven that HIV's main target is active CD4 T cells [3], the mechanism of pathogenesis remains unknown. T helper cells (CD4+ T cells) are the most well-known and studied immune cells in HIV research since they are the main targets for HIV. The loss of these vital immune cells is a hallmark of HIV infection and contributes to the clinical manifestations that characterize AIDS [4, 5]; however, whether these T cells are lost directly or indirectly in HIV-infected people is a point of contention. Nonetheless, the loss of these T cells compromises immunity, resulting in opportunistic infections as well as malignancies in HIV-positive people [6]. HIV depletes the whole host cell CD4+ T-cell pool via interactions with CD4 and the chemokine co-receptors, CCR5 or CXCR4 [7]. HIV is a major global public health concern, having claimed the lives of almost 36.3 million people thus far [8]. In 2020, 680 000 persons died from HIV-related causes worldwide. At the end of 2020, there were estimated 37.7 million people living with HIV (PLHIV), with 1.5 million people newly infected with Africa accounting for about 60% of all new HIV infections worldwide [9]. The infection is spread by sexual contact, sharing intravenous drug paraphernalia, and mother-to-child transmission (MTCT), which can occur during the birthing process or during breastfeeding. It is also spread through contact with infected body fluids such as blood, breast milk, sperm, and vaginal secretions [9]. Nevertheless, it is increasingly becoming a known fact that some people have had repeated unprotected sexual encounters with their infected partners and yet did not get the infection. This condition called HIV discordance is a situation that occurs when one partner is HIV positive and the other is HIV negative [10]. Previous research has shown that HIV discordant couples are a high-risk group for HIV transmission [11]. Notably, in Africa, there is

increasing evidence that a large proportion of new HIV infections occur in cohabiting couples [12]. In Nigeria, the presences of HIV exposed seronegative subjects among discordant partners have been reported [12, 13]. Infection with the HIV and subsequent antiretroviral therapy (ART) are frequently associated with lipid profile changes. Despite the fact that antiretroviral therapy suppresses viral replication, prolonged inflammation is expected to cause changes in lipid composition and function, increasing the risk of cardiovascular disease [14]. Several studies have observed significant alterations in lipid profile levels among HIV positive individuals who are either on ART or are naïve [15,16]. Although antiretroviral medication has lowered mortality and changed HIV infection into a chronic condition; yet, ART usage has been linked to lipid abnormalities and lipodystrophy [17, 18], although some other studies documented different results [2].

There abound many HIV positive and HIV exposed sero-negative subjects in Nigeria including long term non-progressors with HIV positive partners. Some of these subjects are naïve while some are not and are placed on ART treatment to further help protect them. Given that this group of people (seronegative HIV-exposed individuals) is at high risk of contracting HIV from their partners, and that HIV infection and subsequent ART are frequently linked to changes in lipid profile levels, the importance of investigating biochemical indices like lipid profile levels in this group of people in Nigeria cannot be overstated. The study being the first of its kind in Plateau State, Nigeria is aimed at investigating potential changes in lipid profile levels of HIV serodiscordant couples in Nigeria. The results of the study will be of immense importance to health workers and HIV-related policy makers, as well as for the management of the health of people living with HIV.

## **MATERIALS AND METHODS**

### **Study Area and Location**

The study area for this work was Jos North Local Government Area of Plateau State and location includes APIN (Aids Preventive Initiative of Nigeria) section of Our Lady of Apostles (OLA) Hospital, Faith Alive Foundation Hospital and Plateau Specialist Hospital all based in Plateau state, Nigeria where HIV screenings were carried out.

### **Study Design and Subject Selection**

A cross sectional study approach was adopted for the present study. The subjects include known HIV positive and their exposed but negative partners within the age range of 18 to 49 years of age. Also, apparently healthy aged matched HIV negative couples were used as control. The HIV positives were already on drug while their negative partners in discordant relationship were not on ART.

### **Study Population**

The study population included male and female subjects in discordance relationship within the age of 18 to 49 years attending the APIN section of Our Lady of Apostles Hospital, Faith Alive Foundation and Plateau State Specialist Hospital. A total of 20 discordant HIV couples (40 patients) and 20 controls (40 non HIV couples) were included in the study.

### **Sample Collection**

Five milliliters (5ml) of fasting venous blood sample was collected after sterilizing the site of collection with 70% alcohol into plain containers and allowed to clot, retracted and serum

obtained after centrifugation at 3,000 rpm for 5 minutes. Serum samples that were not analyzed immediately were stored frozen at -20°C.

### **Inclusion criteria**

Participants aged between 18 and 49 years and who were registered HIV patients with proper documentation of status at the hospitals of investigation were included in the study. The spouses of the participants who were found to be HIV negative and in a stable discordant relationship for at least 3 months and above were included. Also age-matched apparently healthy participants were included in the study as control group (non HIV subjects).

### **Exclusion Criteria**

Participants who are already down with AIDS and bed ridden or had other health complications; individuals who were not registered patients or properly documented with the hospitals of investigation as well as those who failed to provide informed consent and did not present themselves for follow ups were excluded from the study.

### **Laboratory methods**

Total cholesterol (TC), triglyceride (TG), and high density lipoprotein cholesterol (HDL-C) concentrations were assayed using enzymatic methods [19, 20, 21]. Low density lipoprotein cholesterol (LDL-C) concentration was calculated using the formula described by [22], while very low density lipoprotein cholesterol (VLDL-C) concentration was determined as TG/5.

### **Statistical Analysis**

The data obtained were analyzed using independent t-test and one-way analysis of variance (ANOVA) with the aid of SPSS statistics tool version 23.0 software. Significant level was assumed at  $p < 0.05$ .

## Results

There were significantly higher mean serum levels of TG, VLDL-C and LDL-C than in control, but HDL-C levels was significantly lower in the HIV discordant test group compared to control group ( $p < 0.05$ ) whereas the mean serum TC level was not significantly different in the HIV discordant test group than in the control ( $p = 0.211$ ). See table 1.

When comparing the mean serum TC levels within the groups ( $p > 0.05$ ) and between the groups ( $p > 0.05$ ), no significant differences were found. (See table 2). The male test group's mean serum TG levels were significantly higher than the male control and female control groups ( $p = 0.001$ ). The mean serum TG level obtained in the male test group, on the other hand, did not differ significantly from the observed values in the female test group ( $p > 0.05$ ). (See table 2). The female test group's mean serum HDL-C level was significantly lower than the female and male control groups ( $p = 0.000$ ). In addition, the male test group's mean serum HDL-C level was significantly lower than the female and male control groups ( $p = 0.000$ ), respectively. (See table 2). Nonetheless, when comparing the male and female test groups, the difference in the mean serum HDL-C level was not statistically significant ( $p > 0.05$ .) (See table 2). Furthermore, the mean serum VLDL-C level in the male test group was significantly higher (0.002) than in the male control and female control groups, but did not differ significantly from the value seen in the female test group ( $p > 0.05$ ). (See table 2). Also, when comparing the groups studied, the difference in mean serum LDL-C levels was not statistically significant ( $p > 0.05$ ), except for the

values observed in the female test group, which were significantly higher than the female control group ( $2.85 \pm 1.24$  Vs  $1.71 \pm 0.35$ ;  $p=0.001$ ). (See table 2).

The difference in mean serum levels of Triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and very low density lipoprotein cholesterol (VLDL-C) were statistically significant among the groups (f-value=3.499, 8.316, 4.185, and 3.284) ( $p < 0.05$ ), respectively, according to analysis of variance, whereas the mean serum total cholesterol level did not differ significantly (f-value=2.302;  $p=0.053$ ). See table 3.

The mean serum total cholesterol levels between the tested groups did not differ significantly ( $p > 0.05$ ) in a paired wise comparison. (See table 3.). The male HIV exposed seronegative participants' mean serum TG levels ( $1.58 \pm 0.53$ ) were significantly higher than the female control ( $1.05 \pm 0.13$ ) and male control group ( $1.13 \pm 0.17$ ) ( $p=0.007$ ), but did not differ significantly from the female seropositive, HIV exposed seronegative female, and HIV seropositive male participants' values ( $p > 0.05$ ). (See table 3.). The discordant HIV positive female's mean serum HDL-C level was significantly lower ( $0.93 \pm 0.27$ ) than the values observed in both female ( $1.40 \pm 0.43$ ) and male control participants ( $1.36 \pm 0.34$ ) ( $p=0.000$ ). When compared to the values observed in the female ( $1.40 \pm 0.43$ ) and male control participants ( $1.36 \pm 0.34$ ), the mean serum HDL-C level in the discordant HIV exposed seronegative female ( $0.79 \pm 0.17$ ) was significantly lower ( $p=0.000$ ). The discordant HIV exposed seronegative male individuals' mean serum HDL-C level was significantly lower ( $0.90 \pm 0.29$ ) as compared to the female ( $1.40 \pm 0.43$ ) and male control participants ( $1.36 \pm 0.34$ ), respectively ( $p=0.000$ ). However, when comparing the groups, the difference in mean serum HDL-C level in male discordant HIV positive participants was not statistically significant ( $p > 0.05$ ), (See table 3). Except for the values reported in the male HIV exposed seronegative participants, which were significantly higher than the female control group

( $0.32 \pm 0.11$  Vs  $0.20 \pm 0.05$ ;  $p=0.010$ ), the difference in mean serum VLDL-C level was not statistically significant between the groups tested ( $p>0.05$ ). (See table 3). Also, when comparing the groups tested, the difference in mean serum LDL-C levels was not statistically significant ( $p>0.05$ ), except for the values observed in the female HIV positive participants, which were significantly higher than the female control group ( $2.95 \pm 1.36$  Vs  $1.71 \pm 0.35$ ;  $p=0.002$ ). (See table 3).

**Table 1: Lipid profile levels in the HIV discordant test group and control (Mean $\pm$ SD).**

Parameter	Control group (n=40)	Discordant HIV Test group	t-value	p-value

		(n=40)		
TC (mmol/L)	3.88±0.56	4.12±1.05	1.262	0.211
TG (mmol/L)	1.09±0.16	1.43±0.57	3.621	0.001*
HDL-C (mmol/L)	1.38±0.38	0.90±0.26	6.529	0.000*
VLDL-C (mmol/L)	0.21±0.06	0.28±0.11	3.492	0.001*
LDL-C (mmol/L)	1.96±0.57	2.59±1.11	3.159	0.002*

\*Statistically significant at  $p < 0.05$ .

**Table 2: Levels of lipid profile in the male and female HIV discordant group (mean±SD)**

Parameter	Female	Male	Female test	Male test	f-value	p-value
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	control (n=11)	control (n=12)	(n=21)	(n=22)		
TC (mmol/L)	3.64±0.36	4.18±0.63	4.31±1.24	3.93±0.81	4.53	0.070
TG (mmol/L)	1.05±0.13	1.13±0.17	1.31±0.57	1.55±0.56 <sup>a,b</sup>	5.715	0.001*
HDL-C (mmol/L)	1.40±0.43	1.36±0.34	0.90±0.25 <sup>a,b</sup>	0.91±0.27 <sup>a,b</sup>	13.941	0.000*
VLDL-C (mmol/L)	0.20±0.05	0.22±0.07	0.26±0.11	0.31±0.11 <sup>a,b</sup>	5.411	0.002*
LDL-C (mmol/L)	1.71±0.35	2.22±0.64	2.85±1.24 <sup>a</sup>	2.33±0.93	5.970	0.001*

\*Statistically significant at  $p < 0.05$ ; Key: a=compared with female control; b=compared with male control.

**Table 3: Lipid profile levels in the groups studied (mean± SD)**

Parameter	Female	Male	Female	Female	Male	Male	f-	p-
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	control (n=20)	control (n=20)	positive (n=16)	negative (n=4)	positive (n=4)	negative (n=16)	value	value
TC (mmol/L)	3.64±0.36	4.13±0.63	4.45±1.35	3.77±0.32	4.40±0.67	3.81±0.82	2.302	0.053
TG(mmol/L)	1.05±0.13	1.13±0.17	1.34±0.53	1.20±0.82	1.45±0.76	1.58±0.53 <sup>a,b</sup>	3.499	0.007*
HDL-C (mmol/L)	1.40±0.43	1.36±0.34	0.93±0.27 <sup>a,b</sup>	0.79±0.17 <sup>a,b</sup>	0.93±0.19	0.90±0.29 <sup>a,b</sup>	8.316	0.000*
VLDL-C (mmol/L)	0.20±0.05	0.22±0.07	0.26±0.10	0.24±0.16	0.29±0.15	0.32±0.11 <sup>a</sup>	3.284	0.010*
LDL-C (mmol/L)	1.71±0.35	2.22±0.64	2.95±1.36 <sup>a</sup>	2.44±0.21	2.82±0.69	2.20±0.96	4.185	0.002*

\*Statistically significant at  $p < 0.05$ ; Key: a=compared with female control; b=compared with male control.

## Discussion

Infection with the human immunodeficiency virus (HIV) is one of the most challenging health issues to confront in the last three decades, as it affects a large fraction of the world's population [23]. The current study looked at the lipid profiles of HIV serodiscordant couples in Jos, Plateau State, Nigeria.

In this investigation, the HIV discordant test group had significantly higher serum TG, VLDL-C, and LDL-C levels than the control, whereas HDL-C values were significantly lower. The differences in mean serum TC levels were not statistically significant. Several investigations indicated significant lipid profile modifications, including a decrease in HDL-C and an increase

in mean serum TC, TG, LDL-C, and VLDL-C [24, 25]. Other research found HIV-infected and AIDS patients had lower total cholesterol and LDLs but higher triglycerides and very LDLs than seronegative controls which partly agreed with the present finding [15]. HIV discordant persons are at risk for cardiovascular disease and need therapeutic intervention and lipid profile monitoring. The change in lipid profile may be due to antiretroviral medication or impaired immunity, making patients prone to infections. Some other studies have observed varying prevalence of dyslipidemia in HIV infected individuals [26].

Furthermore, the mean serum TC levels in the male and female HIV serodiscordant test groups were not statistically different from the male and female control groups in this investigation. This result is consistent with the findings of Njoroge *et al.* [27], who found no significant difference in mean total cholesterol levels between HIV-positive and HIV-negative people. Thus, contrary to some previous HIV research, which revealed that HIV positive individuals had significantly lower TC levels than controls [15], this study found no significant alteration in TC levels in both male and female HIV positive compared to control discordant partners. Nevertheless some other investigations reported HIV patients had significantly higher TC levels than controls [28].

The mean serum TG levels of the male HIV serodiscordant test group were significantly higher than in the male control and female control groups. On the other hand, the mean serum TG level in the male HIV discordant test group did not differ significantly from the observed values in the female HIV serodiscordant test group. Elevated serum triglyceride level is an important risk factor for cardiovascular disease. Triglycerides (TGs) are nonpolar lipid molecules made up of a glycerol molecule linked to three fatty acid (FA) molecules, and they constitute the body's primary source of lipid storage and energy [29, 30]. The traffic of TGs in specific tissues, such as muscle, liver, and adipose tissue, is a biological process that is essential for life. They are

synthesized primarily through the glycerol phosphate pathway, and the traffic of TGs in specific tissues, such as muscle, liver, and adipose tissue, depends on the nutritional state of the individual. Hypertriglyceridemia and lipotoxicity are among metabolic diseases that can be caused by an imbalance in this mechanism. Hypertriglyceridemia may play a role in the development of atherosclerosis through unknown mechanisms. Atherosclerosis is an inflammatory disease affecting the arterial wall that leads to myocardial, cerebral, and peripheral ischemic syndrome [29]. Several factors have been adduced to contribute to rise in triglyceride level in HIV infected participants. Infections have been suggested to raise plasma triglyceride levels by reducing the clearance of circulating lipoproteins, a process thought to be caused by reduced lipoprotein lipase, or by stimulating hepatic lipid synthesis through increases in either hepatic fatty acid synthesis or reesterification of fatty acids derived from lipolysis [31]. In HIV-infected patients, serum triglycerides levels rise as the disease advances, especially when opportunistic infections are present. Furthermore, inflammation and infections enhance the production of cytokines that affect lipid metabolism, such as tumor necrosis factor-alpha (TNF-), interleukin (IL)-1, and IL-6 [30]. Acute cytokine administration causes many of the alterations in plasma lipids and lipoproteins that are found during chronic inflammation and infections [32]. Several cytokines (TNF-, IL-1, IL-2, IL-6, and others) increase TG and VLDL-C blood levels [31, 30]. The rise in serum TGs is attributed to an increase in hepatic VLDL-C production and secretion as a result of increased hepatic FA synthesis and the resulting decreased clearance of TG-rich lipoproteins. These modifications, when combined, result in an increase in fatty acid supply to the liver, which increases hepatic TG production [30]. The clearance of TG-enriched lipoproteins is reduced. Previous studies have shown elevated levels of TG in HIV infected persons than in control [25, 15] which agrees with the current result.

In this study, both male and female HIV discordant couples had significantly lower HDL-C values than male and female control individuals, respectively. The level of HDL-C recorded in this participants meet the criteria for dyslipidemia as defined by the National Cholesterol Education Program (NCEP-ATP III), with mean serum level of less than 1.03mmol/l [33]. Because HDL is the principal carrier of cholesterol from peripheral tissues to the liver, it plays a vital role in reverse cholesterol transport and cholesterol balance. HDL is regarded as the beneficial micelle in the lipoproteins family contrary to LDL due to the reverse cholesterol transport function of HDL. Apart from reverse cholesterol transfer, HDL also plays a role in LDL anti-oxidation, vasodilation, anti-thrombosis, cell apoptosis reduction, and anti-inflammation [34]. The male and female HIV serodiscordant couples are at risk of cardiovascular disease if timely interventional therapy is not commenced as a result of this decrease in HDL-C levels. Low levels of high-density lipoprotein cholesterol (HDL-C) are linked to an increased risk of coronary artery disease (CAD), whereas high levels of HDL-C are linked to a lower risk of CAD and myocardial infarction [35]. This decline could be due to the use of antiretroviral therapy (ART) or it could be the result of the HIV infection itself. In HIV naive persons as well as HIV positive individuals on ART, studies have found similar results to the findings in the current study when compared to seronegative individuals [27, 25].

Furthermore, the mean serum VLDL-C level in the male HIV serodiscordant test group was significantly higher than in the male control and female control groups, but did not differ significantly from the value seen in the female test group. Increased tumor necrosis factor and other cytokines that occur during the infection promote lipolysis and insulin resistance, according to Iffen *et al.* [24]. This is the likely reason for the increase in triglycerides and VLDL cholesterol levels in their study. Insulin controls glucose uptake in skeletal muscle tissue and

other cells throughout the body. Increased free fatty acids in the circulation and reduced storage of triglycerides in the adipose tissues occur as insulin sensitivity declines in HIV-infected patients with decreased CD4 cell counts and uptake of glucose into skeletal muscle tissue and other cells. These free fatty acids are delivered back into circulation as triglycerides by the liver. As a result, HIV-positive people have much greater triglyceride levels than HIV-negative people. VLDLs are primarily made up of triglycerides. When triglycerides rise, VLDL rises as well. The present result is in keeping with the report of Nayyar [15]. In general, the study found no significant difference in lipid profile levels between male and female serodiscordant subjects. This reveals that gender variations did not affect lipid profile changes between discordant HIV participants. This contrasts with Ezeugwunne and colleagues, who found lower TC, LDL-C, and HDL-C levels in male HIV-infected patients than in female HIV-infected participants [36]. Surprisingly, when comparing the groups studied, mean serum LDL-C levels did not differ significantly except for the values observed in the female test group, which were significantly higher than the female control group. This may imply that the female HIV discordant group is at a greater risk of cardiovascular disease if left unmanaged. Several studies have shown higher levels of LDL-C in HIV infected individuals [25]. LDL-C is thought to be a key risk factor for revascularization, ischemic strokes, atherothrombotic disease, and cardiovascular mortality [37]. Increased LDL-C promotes atherosclerosis by causing cholesterol and fatty acid accumulation in the arterial wall, whereas HDL-C is thought to be beneficial by returning cholesterol to the liver [38, 39].

In this study, male HIV exposed seronegative partners had significantly higher mean serum levels of TG and VLDL-C and lower levels of HDL-C than controls, with no significant changes in mean serum TC and LDL-C. This suggests that the HIV exposed seronegative male partners

may be at risk for cardiovascular disease which may arise due the direct effect of their exposure to the HIV virus present in the positive partners and for whom viral suppression has not been fully attained. Higher TG and VLDL-C levels, as well as lower HDL-C levels, are key biomarkers for cardiovascular disease [40, 41]. Notably, this is the first study of its sort involving the assessment of lipid profile levels in HIV-exposed seronegative partners, making it impossible to compare the current findings to those of other studies.

Surprisingly, the male HIV seropositive partners' lipid profile levels did not differ significantly from the control. This is in contrast to prior research findings, which showed significant changes in lipid profile levels in HIV-positive people [2, 15]. This could be related to the difference in sample size and ART duration.

Furthermore, there were no significant alterations observed in the mean serum TC, TG, VLDL-C and LDL-C levels while significantly lower HDL-C level was observed in the female HIV exposed seronegative partners compared to control. This may suggest that these individuals may be at risk of cardiovascular disease later in life if there is no therapeutic intervention. Low HDL-C level is an independent risk factor for cardiovascular disease [42, 43]. In addition, the female HIV positive partners had statistically significant lower HDL-C and higher LDL-C levels with no significant changes in TC, TG, LDL-C, and VLDL-C levels, while the female HIV exposed seronegative partners had significantly lower HDL-C levels with no significant differences in TC, TG, LDL-C, and VLDL-C levels. HIV infection has been shown to cause alterations in lipid profile [27, 2].

## **Conclusion**

This study found that HIV serodiscordant couples had significant changes in their lipid profiles, indicating that they may have a higher risk of cardiovascular disease. Furthermore, this study revealed that gender variations did not affect lipid profile changes between discordant HIV participants. Therefore, it is necessary to include a lipid profile test as part of regular checkup measures for these individuals.

### **Ethical Approval**

Ethical approval was obtained from the Ethics Committees of the hospitals: Plateau State Specialist Hospital (PSSH/ADM/ETH.CO/2019/005); Faith Alive Foundation Hospital (FAFEC/08/34/25) and Our Lady of Apostles Hospital (dated 13<sup>th</sup> June, 2018) where the study was carried out.

### **Consent**

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

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