DYSLIPIDEMIA IN PREGNANCY AND ITS CORRELATION WITH PREECLAMPSIA

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ABSTRACT

Objective: To evaluate lipidprofile amongst patients diagnosed with preeclampsia and compare it with normal pregnant patients.

Study Design: Cross-sectional comparative study.

Place and Duration of Study: Obstetrics Unit, Combined Military Hospital Rawalpindi, from Jan to Mar 2021.

Methodology: A total of 80 patients were enrolled and divided into two groups. Group A preeclampsia patients and group B normotensive pregnant patients in third trimester. Inclusion criteria were patients between 20-35 years in third trimester of pregnancy. Patients with preexisting hypertension, diabetes, autoimmune disease and renal problems were excluded. Demographic and reproductive profiles including age, parity, period of gestation and body mass index (BMI) noted. Blood samples after 12 hours of fasting were obtained. Serum total cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL), serum triglycerides and very low density lipoproteins (VLDL) levels calculated. Demographic profile and test results of the two groups were compared. *p*-value of ≤0.05 was considered statistically significant.

Results: A total of 80 patients were enrolled in the study. Mean age of two groups was 28.6 ± 3.8 yrs, mean parity 1.8 ± 1.1, gestational age 33.6 ± 2.6, body mass index 27.7 ± 2. Mean values calculated of the lipid profile of both groups was cholesterol 5.22 ± 1.2, high density lipoproteins 1.68 ± 0.65, low density lipoproteins 3.07 ± 1.1, triglycerides 2.5 ± 0.93, very low density lipoproteins 1.24 ± 0.44. Difference between age, parity, gestational age and body mass index was not significant between the two groups but difference between serum cholesterol and triglyceride levels was significant (p<0.0001).

Conclusion: Our pregnant population generally has raised lipid levels. Women with preeclampsia have lipid profile derangements which are significant in comparison to normotensive patients.

Keywords: Lipid profile, Preeclampsia, Pregnancy.

INTRODUCTION

Normal pregnancy causes physiological changes and alterations in nearly all systems of the body. Lipid metabolism also undergoes changes which are essential for normal fetal development and growth. Starting from first trimester there is accelerated deposition and hypertrophy of adipocytes which is crucial to meet the increasing demands of growing fetus[1]. There is generally increased lipogenesis and reduced lipolysis under the influence of hormones of pregnancy. All this results in increased lipid production which is essential for normal fetal development. With changes in lifestyle more patients now are presenting with cardiovascular disease in pregnancy. Similarly many patients with chronic medical diseases have marked derangement of lipid profiles[2]. Conversely these patients having dyslipidemia have been linked to high perinatal mortality and morbidity. Throughout pregnancy cholesterol and triglycerides rise almost two to four times. Low density lipoproteins are deranged causing atherogenic potential. This rise is not harmful and immediately falls to pre-pregnancy levels after delivery[3]. These changes are more pronounced inwomen with gestational hypertension, preeclampsia and diabetes. These women also have increased risk of developing cardiovascular risk later in life[4].

A recent ABCD study establishes relation of dyslipidemia during early pregnancy with adverse pregnancy outcome including preterm delivery, maternal morbidity and mortality[5]. The exact pathophysiology of this relationship is not completely understood although it is now an area of hot research. Hypertensive disorders in pregnancy are also a leading cause of poor maternal and fetal outcome. Gestational hypertension occurs during pregnancy in which there is increased blood pressure without proteinuria. Preeclampsia (PE) is present in 5-8% of pregnancies and it is defined as new onset hypertension and proteinuria during pregnancy[6]. Many studies have shown deranged lipid concentrations in patients who develop preeclampsia. They usually show increased levels of triglycerides (TG), lower level of HDL and high LDL[7]. All these changes are proatherogenic leading to cardiovascular complications and mild preeclampsia. Patients with severe preeclampsia tend to have low LDL suggesting a different pathologic mechanism. So PE as a comorbid condition

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may accelerate the unfavorable lipid changes and clinical outcomes. Pregnancy is a unique opportunity to detect dyslipidemia as there is very strong emerging evidence that presence of atherogenic lipid profile during early pregnancy leads to adverse pregnancy outcome including hypertensive disorders, gestational diabetes,preterm delivery and large for gestational age fetus. Similarly in these patients there is strong evidence of long term cardiovascular risks later in life and children born to these women are also at increased risk of cardiovascular disease later in life. Hence early detection of dyslipidemia is very important for risk modification and treatment to prevent this complications[8]. There is need for research to define early detection strategies, role of antihyperlipidemic therapies in pregnant women and recommend treatment for significant dyslipidemia in pregnant women. This study was undertaken to determine the lipid profile levels in our pregnant population with preeclampsia and compare it with normal pregnant women.

METHODOLOGY

This cross-sectional comparative study was conducted at Obstetrics and Gynecology department of combined Military Hospital, Rawalpindi, from July 2020 to December 2021. Approval from institutional ethics review committee was obtained. A sample size of minimum 73 cases was calculated with 95% confidence level, 5% margin of error and taking an expected prevalence of preeclampsia as 5%. A total 80 patients were enrolled by nonprobability sampling technique after taking informed consent. They were divided in two groups group A were pregnant patients with preeclampsia and group B were normotensive pregnant patients. Inclusion criteria were women aged 20-35 years, singleton and in their third trimester of pregnancy. Exclusion criteria included high risk pregnancies including those having medical disorders like diabetes, preexisting hypertension, cardiovascular disease, autoimmune disease and renal problems. Demographic and reproductive profiles including age, parity, period of gestation and BMI was calculated. Blood samples after 12 hours of fasting were obtained for calculating lipid profile. Serum total cholesterol, HDL and LDL cholesterol, serum triglycerides and VLDL levels calculated. Demographic profile and test results of the two groups were compared. Preclampsia was diagnosed as blood pressure of 140/90 or more and a spot urine protein creatinine ratio of ≥ 0.2 mg/mg was considered the cut off value for detecting proteinuria. Blood samples were collected after a 12 hour fast. 3ml venous sample was taken in plain tube after centrifugation at 4000 rpm for three minutes. Cholesterol was assayed by CHOL-PAP method on automated chemistry analyser ADVIA 1800. The serum levels were taken asrecommended by National cholesterol education programme (NCEP) ATP III guidelines 2020. Serum cholesterol (desirable <5.2 mmol/L, borderline 5.2-6.2 mmol/L and at risk >6.2 mmol/L, serum HDL cholerterol >1.3 mmol/L, serum LDL cholesterol desirable <2.59 mmol/L, near optimal 2.6-3.34 mmol/L, borderline 3.37-4.12 mmol/L, high risk 4.15-4.9 mmol/L), serum triglycerides (desirable 0.4-1.6 mmol/L, borderline 1.7-2.2 mmol/L, high risk >2.3-5.6 mmol/L and serum VLDL <0.78.

The data was entered and analyzed by SPSS-21. Descriptive statistics was used to calculate mean and standard deviations for age, parity, gestational age and BMI. Lipid profile values were calculated for preeclampsia patients and compared with normal controls. Independent sample t-test andchi-square test was applied and a p-value ≤0.05 was taken as significant.

RESULTS

A total of 80 patients were enrolled in the study. Demographic profile of the two groups was calculated. Mean ageof two groups was 28.6 ± 3.8 yrs, mean parity 1.8 ± 1.1, gestational age 33.6 ± 2.6, body mass index 27.7 ± 2.0. Mean values calculated of the lipid profile of both groups was cholesterol 5.22 ± 1.2, HDL 1.68 ± 0.65, LDL 3.07 ± 1.1, Triglycerides 2.5 ± 0.93, VLDL 1.24 ± 0.44. Nearlly all the values of lipid profile were higher than the normal reference range depicting dyslipidemia in our pregnant population as compared to non-pregnant patients. Difference between age parity gestational age and BMI was not significant between the two groups but serum cholesterol and triglyceride level difference was significant (p<0.0001). BMI in both groups was high showing the obesity trends amongst pregnant population also as shown in table.

Lipid profile reference intervals are shown in figure (a-d). For serum cholesterol in preclampsia group the further categorisation shows majority of patients in moderate risk 22 (55%) wheras amongst normal controls majority were in desirable range 30 (75%). Triglyceride levels were amongst high risk range in 15 (37.5%) patients in preclampsia group and maximum 24 (60%) were in borderline risk group whereas in normal controls maximum were also in borderline range. LDL levels were above optimal in majority of patients in both groups whereas in preeclampsia group 12 (30%) were in high risk range as

compared to 6 (15%) amongst normal pregnat patients. There was very minor difference amongst HDL and VLDL levels in both groups.

Table: comparison of variables between normal pregnant patients and preeclampsia patients.

	Group	N	Mean	SD	*p*-value
Age (year)	Normal patients	40	27.53	3.523	0.007
	Pre-Eclampsia	40	29.85	3.926	
Parity	Normal patients	40	1.90	1.081	0.841
	Pre-Eclampsia	40	1.85	1.145	
Gestational age (weeks)	Normal patients	40	33.35	2.527	0.298
	Pre-Eclampsia	40	33.98	2.806	
Body Mass Index (m^2)	Normal patients	40	27.45	1.999	0.259
	Pre-Eclampsia	40	27.98	2.130	
Cholesterol (mmol/L)	Normal patients	40	4.7513	0.62249	<0.0001
	Pre-Eclampsia	40	5.7082	1.50057	
HDL (mmol/L)	Normal patients	40	1.8752	0.79121	0.010
	Pre-Eclampsia	40	1.5020	0.42513	
LDL (mmol/L)	Normal patients	40	2.8652	1.04266	0.093
	Pre-Eclampsia	40	3.2823	1.14729	
Triglyceride (mmol/L)	Normal patients	40	2.1358	0.84442	<0.0001
	Pre-Eclampsia	40	3.0465	0.78851	
VLDL (mmol/L)	Normal patients	40	1.2792	0.39691	0.485
	Pre-Eclampsia	40	1.2090	0.49327	

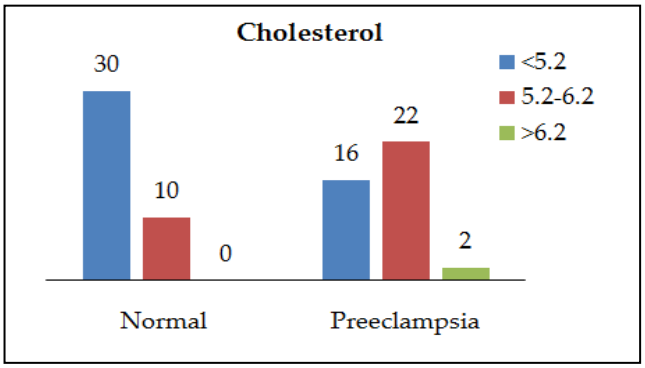


Figure-1A: Cholesterol reference intervals.

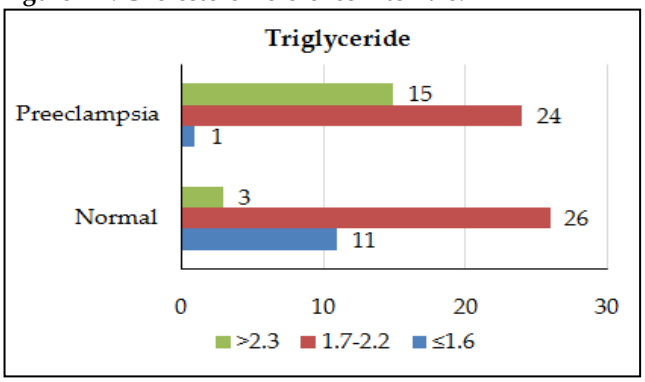
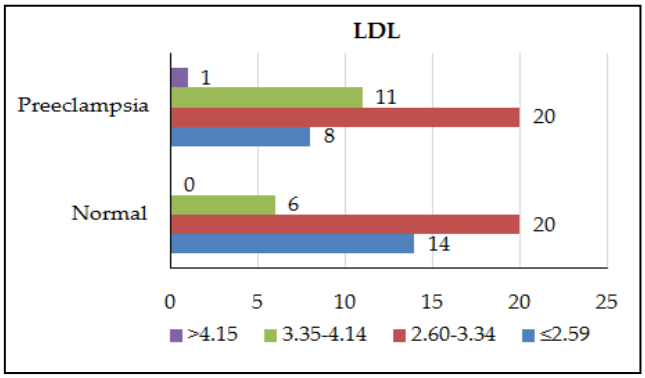


Figure-1B: Triglyceride reference intervals.

DISCUSSION

Preeclampsia is a multi-system disease, manifested by maternal hypertension and end organ damage affecting 3-4% of pregnancies and is associated with high maternal morbidity and mortality[9,10]. Meta-analysis recently performed on research evaluating the relationship between maternal serum triglycerides levels and preeclampsia found that women with preeclampsia had significantly higher levels of triglycerides than normotensive women[11]. Many studies have been done to find out association between maternal serum lipid profiles and pre eclampsia[12]. There have been conflicting results, as some studies show higher lipid profiles in preeclamptic women in comparison to normotensive women and vice versa.In this studymean age was 28.6 ± 3.8 years, mean parity 1.8 ± 1.1, gestational age at testing 33.6 ± 2.6 weeks andbody mass index 27.7 ± 2[13]. Thathagari *et al*, half of pregnant women in pre eclamptic group were in age bracket of 18-25 years while 63% ladies in normotensive group were in this group which is lower than our study participants mean age. In a study done by Avidime *et al*, 38.57% females in preeclamptic group were in 20-24 years age group, while 31.43% normotensive ladies were in this age group. Out of 25% ladies in preeclamptic group were in age bracket of <20 years, while 28.57% in normoten-sive group were of <20 years. 12.86% ladies were in age group of 35-39 years in preeclampsia



Figur-1C: LDL reference intervals.

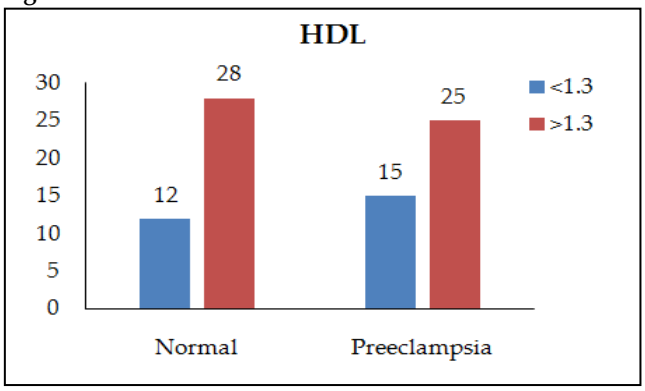


Figure-1D: HDL reference intervals.

group, while 10% ladies in normotensive group were in 35-39 years. This shows women of at all ages can develop pree-clampsia irrespective of other parameters. Out of 51% primigravida were in preeclamptic group and 34% primigravida in normotensive group[14].

In our study mean values of the lipid profile of both groups was cholesterol 5.22 ± 1.2, HDL 1.68 ± 0.65, LDL 3.07 ± 1.1, triglycerides 2.5 ± 0.93 and VLDL 1.24 ± 0.44. Another study showed that proportion of pregnant women with dyslipidemia was more in pre-eclamptic group and it was observed that mean serum total cholesterol levels HDL, LDL VLDL and triglycerides levels were higher than normotensive group and these values were statistically significant. The difference in all lipid parameters other then HDL amongst the two groups was very high[15]. This is quite comparable to our study. In another study by Ahmed *et al*, serum triglycerides was higher in mild preeclampsia while in normotensive group it was lower. The cholesterol levels in severe and mild preeclampsia were raised as compared to normotensive women preeclampsia group. These findings of hypertriglyceridemia and hypercholesterolemia and raised LD/VLDL and decreased HDL are comparable to this study[16]. On the other hand few studies have shown no significant difference in serum levels of maternal lipid profile in pre-eclamptic versus normotensive women. In this study the lipid profile parameters in both groups showed some difference. Normotensive patients had cholesterol 4.75 ± 0.6 (mmol/L), HDL 1.87 ± 0.79 (mmol/L), LDL 2.86 ± 1.04 (mmol/L), triglycerides 2.1 ± 0.84 (mmol/L) and VLDL 1.27 ± 0.39 (mmol/L). whereas in preeclampsia patients cholesterol was 5.7 ± 1.5 (mmol/L), HDL 1.5 ± 0.42 (mmol/L), LDL 3.28 ± 1.1 (mmol/L), triglycerides 3.0 ± 0.78 (mmol/L) and VLDL 1.2 ± 0.49 (mmol/L). In a study by Yeboah *et al*, the lipid profile parameters did not show any significant difference between preeclampsia and normotensive group. The triglyceride level in preeclampsia group was 1.58 ± 0.8 (mmol/L) and 1.61 ± 0.8 (mmol/L) in normotensive patients. Total cholesterol was 6 ± 1.7 (mmol/L) in pre-eclamptic females and 5.8 ± 1.8 in normotensive females. HDL levels were 1.37 ± 10 mmol/l in preeclampsia group and 1.47 ± 0.9 (mmol/L) in normotensive group. LDL was 4.2 ± 1.7 (mmol/L) and 3.9 ± 1.8 (mmol/L) in preeclamptic and normotensive group respectively.

BMI was 32.3 ± 2.7kg/m^2 in preeclamptic group and 25.1 ± 4.1m^2 in normotensive group. This is in contrast to our findings of BMI of 27.7 ± 2kg/m^2 which was similar in both groups. The mean age was 34.5 ± 5.2 yrs in preeclamptic group and 28.6 ± 5.7 years in normotensive group which comparesto our patients in preeclampsia group having advanced age 29.8 ± 3.9 years as compared to normotensive group 27.5 ± 3.5 years. Advanced maternal age and high BMI showed strong relationship with preeclampsia (p<0.0001)[17]. Mean serum triglyceride levels in our study were significantly raised in preeclamptic women in comparison to normotensive pregnant women. Similar findings were reported in other studies[18]. In a study by Mittal *et* al serum triglycerides in mild preeclampsia severe pre-eclampsia and eclampsia as compared to normotensive ladies was increased significantly (p<0.05). Other parameters total cholesterol, HDL and LDL were not changed significantly[19]. In the study done in Nigeria mean serum triglycerides, LDL and VLDL were 2.75 ± 1.25, 3.72 ± 1.05 and 0.55 ± 0.25 mmol/l respectively in the preeclamptic group while their levels in the control group were 1.81 ± 0.55, 2.75 ± 0.94 and 0.36 ± 0.11 mmol/l respectively. The serum levels of triglycerides, LDL, VLDL were significantly higher in preeclamptic group (p<0.001). The mean serum HDL in preeclamptic group was significantly lower 1.29 ± 0.34 mmol/l compared with control group 1.44 ± 0.47 mmol/, similarly in our study it was 1.87 ± 0.7 in normal group and 1.5 ± 0.42 in preeclampsia group[14]. In our study serum triglycerides and cholesterol was higher in pre-eclamptic women as compared to normotensive pregnant females. Similar findings were noted in other studies[20]. Hence estimation of lipid profile in early pregnancy can be considered as a screening method in order to adopt strategies to avoid deleterious effects.

Life style interventions and use of anti-lipidemic therapies in high risk pregnant women can be considered an area of future research. There is paucity of data for use of anti-statins in human pregnancies but there is ongoing debate about the safety and beneficial effects in these high risk patients but quality of evidence for most of the studies is low. More high quality studies are required to improve evidence quality for safe clinical application. Contribution of this study is investigating a neglected area in pregnant females. With the obesity epidemic, sedentary life style and unhealthy eating habits pregnant women should at least receive adequate counseling to urge them to adopt healthier life style and regular checkups according to local guidelines. Limitations are that it is a single center observational study with a small sample size and followup of the patients was not done to study the feto-maternal complications.

CONCLUSION

Our population generally has raised lipid levels. During pregnancy women with preeclampsia have lipid profile derangements in comparison to normotensive pregnant patients which make them prone to obstetric and cardiovascular com-plications. Lipid profile should be done as a routine test during early pregnancy and the patients should be counseled about management strategies for a better maternal and neonatal outcome.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Nasioudis D, Doulaveris G, Kanninen TT. Dyslipidemia in pregnancy and maternal-fetal outcome. Minerva Ginecol 2019; 71(2): 155-62.
2. 2.Alahakoon TI, Medbury HJ, Williams H, Lee VW. Lipid profiling in maternal andfetal circulations in preeclampsia and fetal growth restriction-a prospectivecase control observational study. BMC Pregnancy Childbirth 2020; 20(1): 61-65.
3. 3.Ghodke B, Pusukuru R, Mehta V. Association of Lipid Profile in Pregnancy withPreeclampsia, Gestational Diabetes Mellitus, and Preterm Delivery. Cureus 2017; 9(7): e1420-25.
4. Melchiorre K, Thilaganathan B, Giorgione V, Ridder A, Memmo A, Khalil A. Hypertensive Disorders of Pregnancy and Future Cardiovascular Health. Front Cardiovasc Med 2020; 7(2): 59-62.
5. Vrijkotte TG, Krukziener N, Hutten BA, Vollebregt KC, van Eijsden M, Twickler MB, et al. Maternal lipid profile during early pregnancy and pregnancy complications and outcomes: the ABCD study. J Clin Endocrinol Metabol 2012; 97(11): 3917-3925.
6. Mahmood A, Nusrat. Lipid Profile Abnormalities in Women with Pre-Eclampsia. Ann Pak Inst Med Sci 2017; 13(3): 263-266.
7. Costantine MM, Cleary K, Hebert MF, Ahmed MS, Brown LM, Ren Z, et al. Eunice kennedy shriver national institute of child health and human development obstetric-fetal pharmacology research units network. safety and pharmacokinetics of pravastatin used for the prevention of preeclampsia in high-risk pregnant women: a pilot randomized controlled trial. Am J Obstet Gynecol 2016; 214(6): e1-17.
8. STesfa E, Nibret E, Munshea A. Maternal lipid profile and risk of pre-eclampsia in African pregnant women: A systematic review and meta-analysis. PloS One 2020; 15(12): e0243538-45.
9. Martin JN, Owens MY, Keiser SD, Parrish MR, Tam Tam KB, Brewer JM, et al. Standardized Mississippi Protocol treatment of 190 patients with HELLP syndrome: slowing disease progression and preventing new major maternal morbidity. Hypert Pregn 2012; 31(1): 79-90.
10. Berg CJ, Callaghan WM, Syvenson C, Henderson Z. Pregnancy related mortality in the United States, 1998-2005. Obstet Gynecol 2010; 116(1): 1302-1309.
11. Gallos ID, Sivakumar K, Kilby MD, Thangaratinam S, Vatish M. Pre eclampsia is associated with, and preceded by hypertriglyceridemia: a metanalysis. BJOG 2013; 120(11): 1321-1332.
12. Agrawal V, Gupta BK. Association of lipid profile and uric acid with pre eclampsia of third trimester in Nullipara women. J Clin Diagn Res 2014; 8(7): cc04-07
13. Ghio A, Bertolotto A, Resi V. Triglyceride metabolism in pregnancy. Adv Clin Chem 2011; 55(1): 133-153.
14. Avidine AR, Tella MA, Hadiza G, Abiodua OO. A comparative study of serum lipids levels in pre eclamptic and normotensive pregnant women in a tertiary Hospital, Northwest Nigeria. Biomed J Sci Tech Res 2018, 3(1): 3003-11.
15. Thathagari VC, MVK: Evalution of serum lipids in pre eclampsia: a comparative study. Inter J Reproduc Contracep Obstet Gynecol 2018; 7(4): 1-5.
16. Ahmed AAM, EL Omda FAA, Mousa MSM. Maternal lipid profile as a risk factor for pre eclampsia. Egyptian J Hospital Med 2018, 71(6): 3434-38.
17. Yeboah FA, Ngala RA, Bawah AT, Asare-Anane H, Alidu H, Hamid AM, et al. Adiposity and hyper leptinemia during the first trimester among pregnant women with pre eclampsia. Int J Women Health 2017; 9(1): 449-454.
18. Talayero BG, Sacks FM. The role of triglycerides in atherosclerosis. Currcardial Rep 2011; 13(6): 544-552.
19. Mittal M, Kulkarni CV, Panchonia A, Mittal RK. Evalutaion of serum lipid profile incases of pre eclampsia and eclampsia. Inter J Reporoduc Contracep Obstet Gynecol 2014; 3(3): 732-734.
20. Spracklen CN, Smith CJ, Saftlas AF, Robinson JG, Ryckman KK. Maternal hyperlipidemia and the risk of pre eclampsia. Am J Epidemiol 2014; 180(4): 346-358.