INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

C- REACTIVE PROTEIN AND THE METABOLIC SYNDROME.

Physiology

Dr. Poonam Kalsi	MBBS, MD Physiology, Demonstrator in the PG Department of Physiology, GMC, Jammu.
Dr. Taranjot Kour	MBBS, MD Physiology, Demonstrator in the PG Department of Physiology, GMC, Jammu.
Dr. Vimal Kumar	MBBS, MD Medicine.
Dr. Mrityunjay Gupta	MBBS, MD Physiology, Professor in the PG Department of Physiology, GMC, Jammu.

ABSTRACT

Metabolic Syndrome is a major public health and clinical challenge globally. It comprises a cluster of metabolic abnormalities that include abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, a prothrombotic state and a pro-inflammatory state in the same individual and is associated with an increased risk of vascular events. Various studies have reported that, in recent year's systemic inflammation (measured by high sensitivity C-reactive protein-CRP) - has become an important marker for cardiovascular disease and type 2 diabetes. This prospective observational study was conducted with the aim to determine the association between C- reactive protein and the metabolic syndrome. A total of 60 patients were included in the study. It was observed that the maximum number of subjects studied in case of males i.e., 8 (34.7 %) were in the age group of 41 – 50 years. Whereas, in case of females, maximum number i.e, 15(40.5%) were observed in the age group of 31 – 40 years. Male subjects had a higher mean blood sugar fasting i.e. 121.4 mg/dl than female subjects i.e. 118.02 mg/dl . More than 2/3rd subjects from both the genders were having S. Cholesterol > 200 mg/dl with a comparable mean S. Cholesterol level in both male & female subjects and the mean serum cholesterol in males is 218.0±44.1 and in females mean serum cholesterol is 217±47.8 . The present study further observed that there was a significant association between C-reactive protein and metabolic syndrome (p value=0.001). The present study concluded that C-reactive protein is an important clinical prognostic marker in metabolic syndrome.

INTRODUCTION

Metabolic Syndrome is a major public health and clinical challenge globally. It comprises a cluster of metabolic abnormalities that include abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, a prothrombotic state and a pro-inflammatory state in the same individual and is associated with an increased risk of vascular events.

World Health Organization (WHO) in 1998 firstly describes the criteria for defining metabolic syndrome which consist the insulin resistance or its surrogates (Impaired Glucose Tolerance, IGT or Diabetes) as essential components and at least another two from hypertension, increased triglyceride level, decreased HDL-C level, obesity (increased BMI / waist to hip ratio) and microalbuminuria.[1]

Adult Treatment Panel III (ATPIII) has identified the Five diagnostic criteria and the presence of any three features [central obesity, dyslipidemia (high triglycerides, low HDL), hypertension, and impaired fasting glucose (IFG)] is considered sufficient to diagnose the metabolic syndrome.[2]

Various studies have reported that, in recent year's systemic inflammation (measured by high sensitivity C-reactive protein-CRP) - has become an important marker for cardiovascular disease and type 2 diabetes. It is also observed that high serum CRP is associated with metabolic syndrome.[3]

The significant association between Metabolic Syndrome and CRP has been clearly identified; a Japanese study has re-defined the metabolic syndrome by including High sensitivity C- reactive protein (Hs-CRP) as a component of the definition. According to Datta S et al., (2011), estimation of CRP rather than low density lipoprotein cholesterol (LDL-C) alone could be valuable since the former is an effective marker for heart disease.[4,5]

Thus this prospective observational study was done to determine the association between C- reactive protein and the metabolic syndrome.

Methodology

This prospective observational study was conducted in the Post Graduate Department of Physiology, Government Medical College, Jammu, in 2019 after obtaining approval from the institutional ethical committee.

A total of 60 patients (male and female) attending the Medicine Outpatient Department were involved after obtaining the informed consent from all the patients.

Inclusion Criteria
1. Patients who are willing to participate.
2. Subjects fulfilling the NCEP-ATP III criteria (3 out of 5) of metabolic syndrome, were included in the study.
- **Central Obesity:** Waist circumference: equal to or more than 102 cm in case of males and equal to or more than 88 cm in case of females.
- **Hyper-triglyceridemia:** Triglycerides more than 150 mg/dl (1.7 mmol/L)
- **Low HDL-Cholesterol:** Less than 40 mg/dl (1.03 mmol/L) in case of males and less than 50 mg/dl (1.29 mmol/L) in case of females.
- **Hypertension:** Blood pressure equal to or more than 130/85 mmHg or, on medication for hypertension.
- **Fasting plasma glucose:** Equal to or more than 110 mg/dl (6.1 mmol/L).

Exclusion Criteria:
1. All subjects with age less than 18 years, with known liver disorders, renal disorders, congestive cardiac failure, pregnant women and thyroid disorders were excluded from the study.

Procedure Of Data Collection:
A detailed history and physical examination was done. All the eligible subjects who volunteered to be part of the study were requested to report after overnight fast. Their physical parameters were recorded and their blood samples were collected by the investigator. Blood sample was taken after fasting for 12 hours by patients.

Data was tabulated, organized, analyzed and interpreted in both descriptive and inferential statistics i.e. frequency and percentage distribution, by using statistical package for social science software (SPSS), version 22. Categorical variables were expressed as number and percentage.
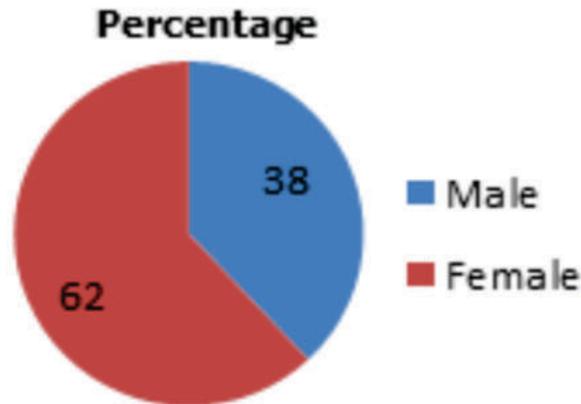
OBSERVATIONS AND RESULT
In this prospective observational study a total of 60 patients were included.

Table- 1 Gender Wise Distribution Of Patients

Male	Female
23 (38%)	37 (62%)

In this present study majority of the participants were females (62%) with the male female ratio 0.62:1 as depicted in table 1.


Percentage

Figure- 1. Gender Wise Distribution Of Patients

Table - 2 Age (in Years)

Age	Male n(%)	Female n(%)
21-30	3(13.0)	2(5.4)
31-40	5(21.7)	15(40.5)
41-50	8(34.7)	12(32.4)
5151-60	7(30.4)	8(21.6)

It was observed that the maximum number of subjects studied in case of males i.e, 8 (34.7 %) were in age group of 41 – 50 years. Whereas, in case of females, maximum number i.e, 15(40.5%) were observed in the age group of 31 – 40 years and the mean age of the male patients was 43.2± 9.12 and the mean age of the females was 42.6± 9.13 as depicted in table 2.
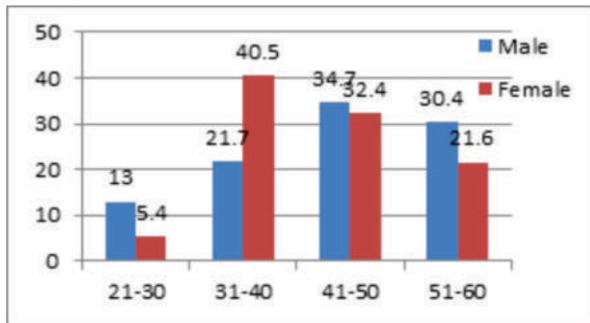

Figure – 2. Age (in years)

Table -3 Weight (in Kgs)

Weight	Male n(%)	Female n(%)
50-70	0(0)	01(2.7)
71-90	6(26.0)	28(75.6)
91-110	16(69.5)	8(21.6)
111-130	0(0)	0(0)
131-150	0(0)	0(0)
151-170	01(4.3)	0(0)

In the present study on an average the male subjects weighed higher than the female subjects with a mean weight of 98.4 kg and 85.4 kg in male and female subjects respectively and the mean weight of the male patients was 98.4± 13.5 kg and the mean weight of the females was 85.4±7.3 kg as depicted in table 3.
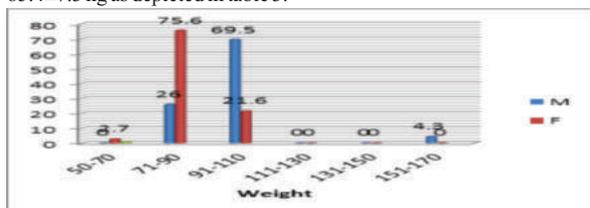

Figure -3. Weight (in Kgs)

Table -4 Height (in cm)

Weight	Male n(%)	Female n(%)
140-149	0(0)	01(2.7)
150-159	4(17.3)	30(81.0)
160-169	14(60.8)	6(16.2)
170-179	5(21.7)	0(0)

In the present study on an average the male subjects were taller than the female subjects with a mean height of 164.8 cm and 155.8 cm in male and female subjects respectively and the mean height of the male patients was 164.8± 5.7 cm and the mean height of the females was 155.8±3.6cm as depicted in table 4.
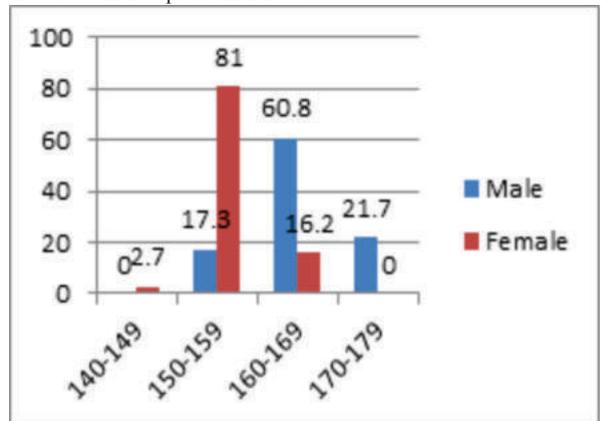
Figure -4. Height (in cm)

Table -5 BMI (Kg/m^2)

Weight	Male n(%)	Female n(%)
<30	0(0)	0(0)
>30	23(100)	37(100)

In the present study all the patients had BMI >30 Kg/m^2 and the mean BMI of the patients was 35.6±3.6 as depicted in table 5.

Table -6. Waist Circumference (cm)

Waist circumference	Male n(%)	Waist circumference	Female n(%)
<102	0(0)	<88	0(0)
>102	23 (100)	>88	37 (100)

All the subjects studied including both males and females were having waist circumference more than the cut off criteria i.e >102 cms in case of males and > 88 cms in females and the mean waist circumference of the male patients was 109± 17.4cm and the mean waist circumference of the females was 95.4±6.4 as depicted in table 6.

Table -7. Hip Circumference (cm)

Hipcircumference	Male n(%)	Female n(%)
91-100	0(0)	18(48.6)
101-110	15(65.2)	15(40.5)
111-120	7(30.4)	4(10.8)
121-130	0(0)	0(0)
131-140	1(4.3)	0(0)
141-150	0(0)	0(0)

It was found that hip circumference was higher in male subjects than female subjects with a mean of 112.0 cm and 103.0 cm in male and female subjects respectively and the mean hip circumference of the male patients was 112± 6.09 cm and the mean hip circumference of the females was 103.0±6.4 cm as depicted in table 7.

Table -8. Blood Sugar (fasting In Mg/dl)

Blood sugar (mg/dl)	Male n(%)	Female n(%)
<110	6(20)	2(5.4)
>110	17(73.9)	35(94.5)

Male subjects had a higher mean blood sugar fasting i.e, 121.4 mg/dl than female subjects i.e, 118.02 mg/dl as depicted in table 8.

Table-9 Serum Cholesterol (mg/dl)

Blood sugar (mg/dl)	Male n(%)	Female n(%)
<100	0(0)	0(0)

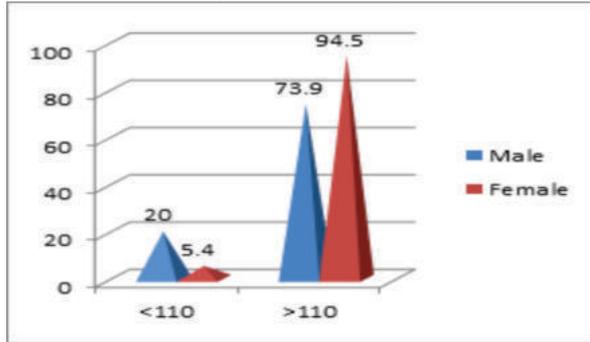|		
100-200	7(30.4)	12(32.4)
>200	16(69.5)	25(67.5)

Figure 5. Blood Sugar (fasting in mg/dl)

In this study more than $2/3^{rd}$ subjects from both the genders were having S. Cholesterol > 200 mg/dl with a comparable mean S. Cholesterol level in both male & female subjects and the mean serum cholesterol in males is 218.0±44.1 and in females mean serum cholesterol is 217±47.8 as depicted in table 9.
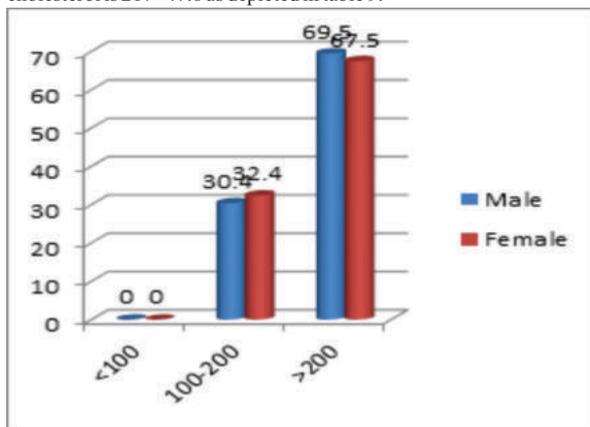

Figure- 6. Serum Cholesterol (mg/dl)

Table- 10 C- Reactive Protein (mg/l)

C-reactive protein (mg/l)	Male n(%)	Female n(%)
<2.0	2(8.6)	4(10.8)
2.0-6.0	15(65.2)	23(62.1)
>6.0	6(26.0)	10(27.0)

The present study revealed that 15 male subjects (65.2%) were having C – Reactive protein level in the range of 2.0 – 6.0 mg/L and 6 (26%) having > 6 mg/L. In case of females subjects 23 (62.1%) were having C - reactive protein level in the range of 2.0 – 6.0 mg/L and 10 (27%) having > 6 mg/L. The mean C-reactive protein in male was 5.2±4.1 and in females 5.7±5.4 as depicted in table 10.
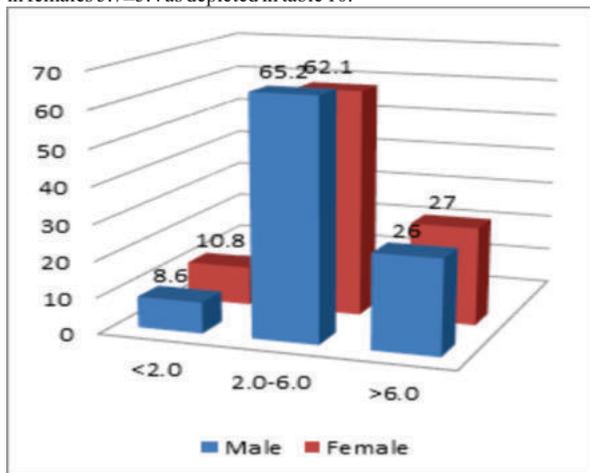

Figure 7. C- Reactive Protein (mg/l)

Table- 11 Systolic Blood Pressure (mmHg)

Systolic blood pressure (mmHg)	Male n(%)	Female n(%)
<130	1(4.3)	5(13.5)
>130	22(95.6)	32(86.4)

22 male subjects (95.6%) were having SBP ≥ 130 mmHg and 1(4.3%) having < 130 mmHg. 32 (86.4%) females were having SBP ≥ 130 mmHg and 5 (13.5%) having < 130 mmHg. The mean systolic blood pressure among male was 148.26±9.21 and in female 142.24±14.33 as depicted in table 11.
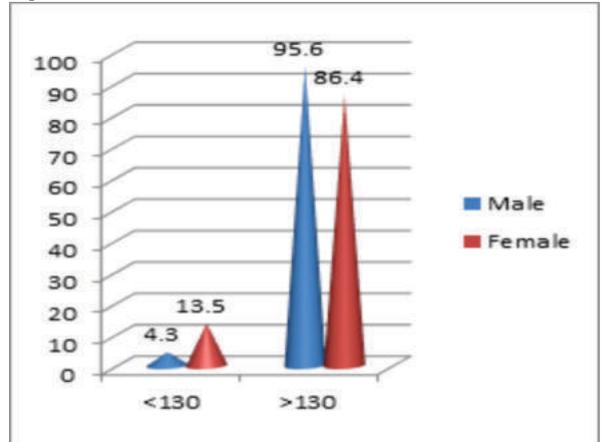

Figure 8 . Systolic Blood Pressure (mmHg)

Table- 12 Diastolic Blood Pressure (mmHg)

Diastolic blood pressure (mmHg)	Male n(%)	Female n(%)
<85	1(4.3)	7(18.9)
>85	22(95.6)	30(81.08)

22 male subjects (95.6%) were DBP ≥ 85 mmHg and 1 (4.3%) having < 85 mmHg and 81% females were having DBP ≥ 85 mmHg and the mean diastolic blood pressure among male was 91.04±3.66 and in female 88.49±5.63 as depicted in table 12.
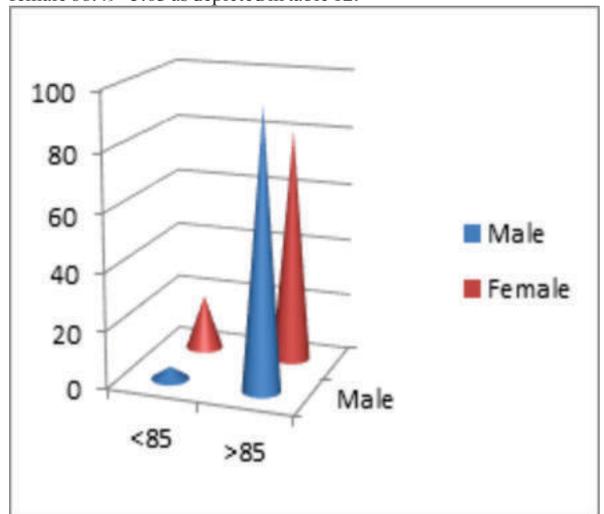

Figure 9 . Diastolic Blood Pressure (mmHg)

The present study further observed that there was a significant association between C-reactive protein and metabolic syndrome (p value=0.001).

DISCUSSION
In this study 60 patients, who were clinically diagnosed with metabolic syndrome manifestations were included. Detailed examinations and investigations were carried out in all the cases. Data was analyzed and discussed with previous literature.

In the present study, out of 60 subjects, who were examined, 23 (38%) were males and 37 (62%) were females, with male: female ratio of

0.62:1. This was similar to the observations by (Shantha GPS et al., 2009). [6]

Age of the participant ranged of between 18-60 years with combined mean age of 42.8 ± 9.06 yrs. Similarly a study conducted by Gutch M et al., 2017, reported that mean age of the participants was 38.10 ± 10.33 years (range = 19-60 yrs). [7]

The combined mean weight of subjects was 90.4 ± 11.9 kgs and 100% subjects in our study were obese which is supported by a study conducted in North part of India (Gutch M et al., 2017). [7]

The combined mean height of subjects in our study was 159.2 ± 6.3 cms the findings are supported by the study conducted by Taki K et al., 2008. [5]

A similar study conducted by Shah P et al., 2017 included the subjects with mean BMI of 31.51 ± 5.21 kg/m^2, it supports our study, which has combined mean BMI of 35.6 ± 3.6 kg/m^2. [8]

The waist circumference was 102 cm and 88 cms in male and female respectively. These findings are supported by a study conducted in Vadodara (Shah P et al., 2017), which included male and female subjects having waist circumference more than the cut-off values i.e. 100% and 90% respectively. Combined mean waist hip ratio (WHR) was 0.94 ± 0.017 in our study group which is correlated with the study conducted by Shah P et al., 2017 , showed that waist hip ratio was 0.97 ± 0.094. [8]

A Japanese study conducted by Taki K et al., 2008 observed that, the mean fasting blood sugar of 112 ± 28 mg/dl which is similar to our study which had combined mean FPG of 119.3 ± 16.2 mg/dl. [5]

The mean serum cholesterol level was 217.8 ± 47.8 mg/dl in present study and this observation is in accordance with a study which had a mean serum cholesterol of 225.9 ± 26.7 mg/dl (Shantha GPS et al., 2008). [6]

Systemic inflammation is closely involved in the pathogenesis of metabolic syndrome (Ferroni P et al., 2004). Several clinical studies have demonstrated that CRP was increased in subjects with metabolic syndrome (Ford ES, 2003). Mean CRP was 5.5 ± 4.9 mg/L with mean CRP of 5.2 ± 4.1 mg/L and 5.7 ± 5.4 mg/L in male and female subjects respectively with a statistically non-significant difference between them (p = 0.67). CRP levels were slightly higher in female than in male subjects in our study and the same was observed in a study conducted by Rutter MK et al., 2004. [9,10,11]

The mean SBP was 144.0 ± 12.81 mmHg. The mean SBP in male subjects was slightly higher (148.26 ± 9.21) mmHg than female subjects (142.24 ± 14.33) mmHg with a statistically significant difference between them (p = 0.025). Clinically, greater importance is attached to diastolic blood pressure (DBP) because this much pressure is being exerted all the time during systole and diastole, Since a sustained high pressure causes damage to the vessel walls, so diastolic hypertension is much more dangerous than systolic hypertension (Ghai CL, 2013). [12]

CONCLUSION
In this prospective observational study a total of 60 patients diagnosed with metabolic syndrome were included. A detailed examination was done and the present study concluded that C-reactive protein is an important clinical prognostic marker in metabolic syndrome.

REFERENCES
1. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome- a new worldwide definition. *Lancet* 2005; 366: 1059-62.
2. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) *JAMA*. 2001;285:2486–2497.
3. Sattar N, McConnachie A, Shaper AG, Blauw GJ, Buckley BM, de Craen AJ, et al. Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. Lancet. 2008, 371: 1927-1935.
4. Datta S, Iqbal Z, Prasad KR. Comparison between serum Hs-CRP and LDL cholesterol for search of a better predictor of ischemic heart disease. *Indian J Clin Biochem* 2011; 26: 210-3.
5. Taki K, Nashio K, Hamajima N, NiwaT. Metabolic syndrome defined by new criteria in Japanese is associated with increased liver enzymes and C- reactive protein. *Nagoya J Med Sci* 2008; 70(1): 1-9.
6. Shantha GPS, Kumar AA, Jeyachandran V, Rajkumar K, Salim S, Subramanian KK, et al. Association between primary hypothyroidism and metabolic syndrome and the role of C reactive protein: A cross-sectional study from South India. *Thyroid Res* 2009; 2: 2
7. Gutch M, Rungta S, Kumar S, Agarwal A, Bhattacharya A, Razi SM. Thyroid functions and serum lipid profile in metabolic syndrome. *Biomed J* 2017; 40(3): 147-53
8. Shah P, Patel H, Dosi R. Subclinical hypothyroidism in metabolic syndrome and role of CRP in 50 adult patients. *J Evid Based Med Healthc* 2017; 4(33): 1960-67
9. Ferroni P, Basili S, Falco A, Davi G. Inflammation, insulin resistance and obesity. *Curr Atheroscler Rep* 2004; 6: 424-31
10. Ford ES. The metabolic syndrome and C-reactive protein, fibrinogen and leukocyte count: findings from the Third National Health and Nutrition Examination Survey. *Atherosclerosis* 2003; 168: 351-58
11. Rutter MK, Meigs JB, Sullivan LM, D'Agostino RB Sr, Wilson PW. C- reactive protein, the metabolic syndrome and prediction of cardiovascular events in the Framingham Offspring Study. *Circulation* 2004; 110(4): 380-5
12. Ghai CL. A Textbook of Practical Physiology. 8th ed New Delhi, India: M/s Jaypee Brothers Medical Publishers 2013. pp. 175