# Aetiological Relationship between Nephrotic Syndrome and Mercury – containing Skin Lightening Creams and Medicated Soaps.

\*I.I. Ulasi, \*C.K. Ijoma, O.A. Kalu

### **SUMMARY**

Objective: Drug-induced nephrotic syndrome is common all over the world. Mercury containing skin lightening creams and medicated soaps are probable causes of nephrotic syndrome. This study aims to determine the aetiological relationship between nephrotic syndrome and skinlightening creams and medicated soaps.

Methods: All patients with nephrotic syndrome seen at the renal clinic of UNTH, Enugu over a one-year period from January 1999 to December 1999 were analysed.

Results: Ten patients out of forty-four patients with nephrotic syndrome studied used mercury containing skinlightening creams and medicated soaps giving a prevalence of 22.72%. The mean age was similar for both groups being 25.87  $\pm$  6.6 years in patients who used mercury containing cosmetics and 24.48  $\pm$  9.6 years for the patients who did not use mercury containing cosmetics. Most of the patients who used mercury-containing cosmetics (60%) belonged to the age group of 21 - 30 years as against 38.24% of other patients. The mean 24-hour urinary protein excretion was 12.00gm for patients who used mercury containing skin lightening products and 9.6gm for the other patients. It was noted that the patients who used these products had more massive proteinuria than others, albeit difference not statistically significant. It was significant however, that 70% of patients who used these products had no other precipitating factor. Of the ten patients who used mercurycontaining cosmetics, eight (80%) had remission while 35.29% was documented in the group that did not use mercury containing cosmetics,  $(X^2 = 6.212, p<0.02)$ .

Conclusion: It is concluded that the use of mercury containing skin lightening creams and medicated soaps is associated with nephrotic syndrome in Nigeria. Most patients who use them are unaware of the potential danger of these products. This study highlights the problem, and emphasizes the need for enlightenment of the population at risk. Niger Med J, Vol. 46, No. 2, April – June, 2005: 29-32.

KEY WORDS: Nephrotic syndrome; Mercury; Skinlightening creams; Medicated soaps.

From: \*Renal Unit, Department of Medicine, UNTH, Enugu. Renal Unit, Department of Medicine, NAUTH, Nnewi.

Correspondence: I.I. Ulasi, Renal Unit, Department of Medicine, University of Nigeria Teaching Hospital, Enugu, Nigeria. E-mail: ifeomaulasi@yahoo.co.uk

## INTRODUCTION

Nephrotic syndrome is more common in the tropics than the temperate climate<sup>1,2</sup>. The reasons adduced for this high prevalence include chronic parasitaemia from Plasmodium malariae<sup>3</sup>, and other parasitic infestations like-schistosomiasis<sup>4</sup>, filariasis<sup>5</sup>, leprosy<sup>6</sup>, viral infections<sup>7,8</sup> and use of mercury containing cosmetics<sup>9</sup>.

Nephrotic syndrome from mercury containing drugs was first described in 1947, after the use of organomercurial diuretics in some patients<sup>10</sup>. Since then, there have been several reports of nephrotic syndrome following use of mercury containing compounds topically or systemically<sup>11,12,13</sup>.

The use of cosmetics containing aminomercuric chloride in some parts of East and West Africa has been fashionable in the past two to three decades<sup>13,14</sup>. This has therefore assumed increasing importance as a cause of nephrotic syndrome in the tropics as documented by Bar *et al.*<sup>9</sup>. In the eastern part of Nigeria, light skin complexion is viewed as a mark of beauty. In a study carried out in 1997 by Akpuaka<sup>14</sup>, it was noted that about 50% of women studied used mercury containing skinlightening cosmetics of various forms.

This study was conceived because of the increasing number of persons using mercury-containing cosmetics in the study area. Also, as part of standard protocol in management of nephrotic syndrome and renal disease in the Renal Unit of University of Nigeria Teaching Hospital, history of use of mercury containing cosmetics is always sought and documented. It is a pilot study of patients with nephrotic syndrome, essentially to analyze the prevalence of nephrotic syndrome in patients who use mercury containing cosmetics over a period of one year as a basis for further studies.

## PATIENTS AND METHOD

All patients with nephrotic syndrome seen at the renal clinic of University of Nigeria Teaching Hospital, (UNTH) Enugu over a one-year period from January 1999 to December 1999 were selected. The histories of the patients were reviewed with particular attention paid to use of mercury containing cosmetics and duration of usage. Also history of preceding sorethroat, skin rashes and fever was documented as well as symptoms suggestive of systemic diseases like diabetes mellitus and collagen diseases.

The blood pressure, treatment and response to treatment including remission of these patients were also reviewed. Remission was defined as complete disappearance of oedema and ascitis, and no proteinuria detectable by dipstick.

The results of investigations analyzed included: urinalysis, 24 hour urine protein, serum proteins, serum cholesterol, serum

## I. I. ULASI ET AL.

urea/creatinine, blood film for malaria parasite, viral screen for human immunodeficiency virus/hepatitis B virus and abdominal ultrasonography.

Inclusion criteria: only patients with normal renal function (normal urea/creatinine) were analyzed.

Student t-test, Z score and Chi-square  $(x^2)$  were used for statistical analysis. Level of significant at p < 0.05:

## RESULTS

## Age and Sex

A total of forty-four (44) patients were reviewed (26 males and 18 females; M:F = 1.4:1). Out of these, ten patients i.e. 22.7% (7 males and 3 females; M:F =2.3:1) used mercury containing cosmetics, (Table 1). The duration of usage ranged from six to sixty months with a mean-of twenty-three months. The age range was 16-41 years (mean age  $-25.87\pm6.6$  years) in patients who used mercury containing cosmetics, and 11-50 years for other patients (mean age  $-24.48\pm9.6$  years). Most of the patients who used mercury containing cosmetics (60%) were in the age group 21-30 years as against 38.2% of other patients.

## **Occupation**

Distribution of patients by occupation was similar for both groups ( $x^2 = 1.113$ , p > 0.05). Most of the patients studied were students (50%).

## Blood pressure and hypertension

The mean blood pressure of patients at presentation was higher in those patients who used mercury – containing cosmetics  $(130/85 \pm 21.42/15.09 \text{ mmHg})$  than in the other patients  $(122.91/83.91 \pm 21.07/16.29 \text{ mmHg})$ . Hypertension was found in 30% of the patients who used mercury containing cosmetics as against 44% of other patients, (Table 1).

# Serum protein and 24-hour urinary protein

The mean 24-hour urinary protein was higher in patients

who used mercury containing cosmetics  $(12.00 \pm 8.56 \text{gm})$  than the other patients  $(9.6 \pm 5.15 \text{ gm})$  p > 0.05, not significant. The urinary protein loss was reflected in the serum proteins, (Table 1).

## Kidney size

The mean kidney size as measured by ultrasonography was higher in patients who used mercury containing cosmetics (118.62  $\pm$  15.52 cm) than other patients (113.41  $\pm$  12.87 cm). The difference was not of statistical significance.

## Probable causative factors

Of the patients who used mercury-containing skin lightening cosmetics, 30% (3/10) had history of some infection preceding onset of nephrotic syndrome, out of which one had HBsAg seropositivity. One patient also had history of marijuana abuse and was on anti-psychotic drugs. The remaining 70% (7/10) had no other probable cause except the use of skin lightening cosmetics. Of the thirty-four patients who did not use these cosmetics, 64.71% (22/34) had known probable causes, ( $x^2 = 3.419$ , p was significant). One patient had confirmed human immunodeficiency virus infection while another patient had both vasculitis and scabies.

Malaria parasitaemia of the falciparum species was noted in four of the forty-four patients studied (9.1%). Only one of them used skin lightening cosmetics, (Z=0.112, not significant).

# Response to treatment

The patients who used mercury containing cosmetics responded better to treatment. Eight of them (80%) had long lasting remission, while 35.3% (12/34) was documented in the group that did not use mercury containing cosmetics, ( $X^2 = 6.212$ , p < 0.02). The difference was statistically significant. Of the two patients who used mercury containing products and who did not respond to treatment, one was HBsAg seropositive and had used mercury containing skin lightening products for over sixty (60) months. The other patient had 28.8 gm urinary

Table 1: Characteristics of	Ŀ	Patients	
-----------------------------	---	----------	--

	Patients who used mercury containing cosmetics	Other Patients	P-value
Number of Patients	10	34	> 0.1
Male to Female Ratio	2.3:1	1.3:1	> 0.5
Mean Age (SD) years	25.80 (6.95)	25.21 (10.63)	> 0.5
Mean blood pressure mmHg	/		
Systolic (SD)	130 (20.61)	122 (21.07)	> 0.5
Diastolic (SD)	85 (15.09)	83.91 (16.07)	> 0.05
Prevalence of Hypertension (%)	30	- 44	> 0.5
Mean 24-hour urinary			
protein excretion in gm (SD)	12.00 (8.56)	9.6 (5.15)	> 0.5
Mean serum albumin gm/1 (SD)	24.30 (7.95)	23.03 (10.41)	> 0.5
Mean serum globulin gm/1 (SD)	26.55 (7.18)	30.55 (9.51)	> 0.1
Mean kidney size in mm by			
ultrasonography (SD)	118.62 (15.52)	113.41 (12.87)	> 0.1

## RELATIONSHIP BETWEEN NEPHROTIC SYNDROME AND MERCURY

Table 2: Patients who used skin lightening cosmetics showing duration of usage, response to treatment and other probable causative factors.

Patients	Duration of usage (months)	Response to treatment	Other probable causative factors
1	24	remission	sorethroat
2	6	remission	
3	Occassional usage	remission	
4	60	no remission	HbsAg
5	12	remission	
6	12	remission	
7	8	remission	
8	24	no remission	recurrent sorethroat
9	12	remission	
10	12	remission	

protein excretion/24 hours and also had a history of recurrent sorethroat, (Table 2).

Analysis of patients' treatment showed that twenty-six patients had prednisolone only, one patient had both azathioprine and prednisolone, six patients had both cyclophosphamide and prednisolone. And five patients had been changed from prednisolone to cyclophosphamide on account of side effects and no response.

## DISCUSSION

It is difficult to establish with certainty the aetiological cause of nephrotic syndrome in patients in the tropics as well as in the temperate countries<sup>15</sup>. The use of mercury containing skin lightening products has been documented as a significant cause of nephrotic syndrome in the tropics<sup>9,16</sup>. Bar et al.<sup>9</sup> noted a prevalence of 53.3% (32 of 60 patients), this percentage is way above the prevalence of 22.7% recorded in this present study. This apparent disparity may have several reasons – firstly Bar et al. studied enlightened and fashionable women. In this study, English speaking ability was not an inclusion criterion, the patients studied were from all works of life (they varied from petty traders, students to bankers). Secondly, patients in the study area were reluctant to reveal the use of skin lightening products. It is therefore plausible that some of such patients may have been missed. In a study carried out in the same study area as this one, Akpuaka<sup>14</sup> noted that patients were more likely to give affirmative response if skin/complexion toning cosmetics was used instead of skin lightening or bleaching cream. They also observed that people would give several reasons for selfmedicating with these products. The reasons ranged from skin lesions (dermatoses, acne, eczema) to moisturizing and smoothening of the skin. The male to female ratio of all the patients studied of 1.4:1 is similar to the finding of Adu et al.<sup>2</sup> It is significant that male to female ratio of 2.3:1 was documented for patients who used mercury containing cosmetics however, the male patients (85.71%) were noted to use mercury containing soaps and then skin creams. On the other hand, all the female patients (100%) used both mercury containing skin lightening

soaps and creams. In most studies, use of mercury containing skin lightening cosmetics was limited to women<sup>2,9,13</sup>. In this study, of the seven male patients who used skin lightening products, five (71.47%) used only soaps, one used both and another used only skin cream.

The response to treatment was more remarkable in patients who used these products; eight (80%) had good response to treatment. One patient (10%) had remission upon withdrawal of the offending agents. In contrast, only 35.29% of the other patients who did not use mercury containing cosmetics had good response to treatment. The good response to treatment noted in this study is similar to steroid induced remission seen in other studies<sup>17,18</sup>.

It is concluded that the use of mercury containing skin lightening creams and medicated soaps is strongly associated with development of nephrotic syndrome in Nigeria. Most patients who use them for beauty enhancement are unaware of the potential danger of these agents. This study highlights the problem, and emphasizes the need for enlightenment of the population at risk. It is suggested that doctors practising in black neighbourhoods and Africa should have this in mind and therefore look out for it.

# REFERENCES

- Kibukamusoke J.W., Hutt M.S.R., Wilks N.E. The nephrotic syndrome in Uganda and its association with quartan malaria. *Quarterly Journal of Medicine* 1967; 36: 393 – 408.
- Adu D., Anim-Addo Y., Foli A.K., Blankson J.M., Annobil S.H., Reindorf C.A., Christian E.C. The nephrotic syndrome in Ghana: clinical and pathological aspects. *Quarterly Journal of Medicine* 1981; 50: 297 – 306.
- Hendrickse R.G., Adeniyi A., Edington G.M., Glasgow E.F., White R.G.R., Houba V. Quatan malaria nephrotic syndrome. *Lancet* 1972; i: 1142 – 1149.
- Andrade Z.A., Andrade S.G., Sadigursky M. Renal changes in patients with hepatosplenic schistosomiasis. *American Journal* of Tropical Medicine and Hygiene. 1971; 20: 77 – 82.
- Pillay V.K.G., Kirch F., Kurtzman N.A. Glomerulopathy associated with filarial loasis. *Journal of American Medical*

#### I. I. ULASI ET AL.

- Association. 1973; 225: 179.
- 6. Shure T. Immune complexes in glomeruli of patients with leprosy. *Leprosy Rev.* 1972; **42**: 282 289.
- Editorial. The nephrotic syndrome in the tropics. *Lancet* 1980; ii: 461 – 462.
- 8. Combes B., Shorey J., Barrera A., Stadstay P., Eigenbrodt E.H., Barbera A., Hull A.R., Carter N.W. Glomerulonephritis with deposition of Australian antigen antibody complexes in glomerular basement. *Lancet* 1971; i: 234 237.
- Bar R.D., Rees P.H., Cordy P.E., Kungu A., Woodger B.A., Cameron H.M. Nephrotic syndrome in Adult Africans in Nairobi. British Medical Journal 1972; 2: 131 – 134.
- Derow H.A., Wolff L. Oral administration of mercupurin tablets in ambulatory patients with chronic congestive heart failure. *American Journal of Medicine* 1947; 3: 693.
- Husby G., Tung K.S.K., William R.L. Characteristics of renal tissue lymphocytes in patients with interstitial nephritis. *American Journal of Medicine* 1981; 70: 31 – 38.
- Fillastre J.P., Druet P., Mery J.P. Proteinuric nephropathies associated drugs and substances of abuse. In the Nephrotic Syndrome, (ed. JS Cameron and RJ Glassock), pp 667 – 744. Dekker, New York.

- Kibukamusoke J.W., Davis D.R., Hutt M.S.R. Membranous nephropathy due to skin lightening cream. *British Medical Journal* 1974; ii: 644 – 647.
- 14. Akpuaka M.U. The use of fade creams by women in Enugu chemical, cosmetic and health implications. *Orient Journal of Medicine* 1997; **9**: 44 48.
- Hutt M.S.R. Renal disease in a tropical environment. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1980; 74: 17 – 21.
- Linquist K.L., Makene W.J., Shaba J.K., Nantulya V. Immunofluorescence and electron microscopic studies of kidney biopsies from patients with the nephrotic syndrome, possibly induced by skin lightening creams containing. *East African Medical Journal*. 1974; 51: 168 – 169.
- 17. Becker C.G., Becker E.L., Maher J.F., Shreiner G.E. Nephrotic syndrome after contact with mercury. *Archives of Internal Medicine*. 1962; **110**: 178 186.
- Silverberg D.S., McCall J.T., Hunt J.C. Nephrotic syndrome with use of ammoniated mercury. *Archives of Internal Medicine*. 1967; 120: 581 – 586.