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Range of normal serum immunoglobulin (IgG, IgA and IgM) values in Nigerians

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Summary

The serum levels of immunoglobulins G, A and M of 703 apparently healthy Nigerians resident in Ibadan and aged 1–50 years were studied. The differences in values that are related to age, sex and season were also computed.

Normal values of the immunoglobulins varied with age and sex. IgG mean values for the different age groups ranged from 688 to 1251 mg/100 ml in the males and from 720 to 1038 mg/100 ml in the females. For the IgA class the mean values ranged from 81 to 211 mg/100 ml in the males and from 90 to 206 mg/100 ml in the females. Mean values of IgM varied from 65 to 132 mg/100 ml in the males and from 96 to 114 mg/100 ml in the females.

There was a general increase in IgG levels with advancing age especially in the first 20 years of life. IgA increased progressively with age from 1 to 50 years. The male IgM levels generally rose with increasing age while there was no significant elevation in female IgM values. Females had higher levels of IgG, IgA and IgM in the first 10–20 years of life after which the levels were either the same or higher in the males. The possible reason for this observation is discussed. A significant seasonal influence on the three immunoglobulin concentrations could not be demonstrated.

Résumé

Les niveaux de serum d'immunoglobulines G, A et M de 703 Nigérians apparement sains, domiciliés à Ibadan, et agés de 1 à 50 ans ont été étudiés. Les différences en valeur en fonction de l'âge, du sexe et de la saison ont aussi été calculées.

Les valeurs normales des immunoglobulines variaient avec l'âge et le sexe. Les valeurs moyennes des IgG pour les différents groupes d'âge allaient de 668 à 1251 mg/100 ml chez les hommes et de 720 à 1038 mg/100 ml chez les femmes. En ce qui concerne la classe IgA, les valeurs moyennes allaient de 81 à 211 mg/100 ml chez les hommes et de 90 à 206 mg/100 ml chez les femmes. Les valeurs moyennes des IgM variaient de 65 à 132 mg/100 ml chez les hommes et de 96 à 114 mg/100 ml chez les femmes.

On constatait une élevation générale des niveaux d'IgG à mesure que l'âge avançait et plus particulièrement pendant les 20 premières années de la vie. L'IgA augmentait progressivement en même temps que l'âge de 1 à 50 ans. Les niveaux d'IgM masculins s'élevaient, en règle générale, à mesure que l'âge avançait. Par contre, on ne notait aucune élevation significative des valeurs des IgM féminins. Les femmes avaient des niveaux plus élevés d'IgG, d'IgA et d'IgM pendant les premières 10–20 années de leur vie après quoi les niveaux étaient soit les mêmes qu'avec les hommes, soit plus élevés chez les hommes. La cause possible de ce phénomène a fait l'objet d'un débat. La preuve d'une influence saisonnière significative sur les trois concentrations d'immunoglobulines n'a pas pû être apportée.

Introduction

The works of Milam (1946), Stanier and Thompson (1954), and Edozien (1957, 1961) support the generally accepted fact that serum gamma-globulin levels in persons living in the tropics are higher than in persons living in the

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temperate regions. The most compelling reason to account for the higher levels of the immunoglobulins in tropical populations is the presence of endemic infections in these populations. Apart from environmental conditions (Turner & Voller, 1966; Schofield, 1957; Johansson, Mellbin & Vahlquist, 1968), other factors such as age (Buckley & Dorsey, 1970; Stiehm & Fudenberg, 1966; Allansmith *et al.*, 1968) and sex (McGregor *et al.*, 1970; Berg & Johansson, 1969; Cassidy, Nordy & Dodge, 1974) also influence the levels of serum immunoglobulins in health. It has also been reported that seasonal changes can affect normal levels of the immunoglobulins (McFarlane, 1966). However, Stoop *et al.* (1969) could not demonstrate a consistent seasonal influence on IgG, IgA and IgM.

The necessity for each region to determine its own range of normal values is obvious. Previous reports of immunoglobulin levels in healthy Nigerians have been limited to few subjects (McFarlane, 1966; McFarlane & Voller, 1966) and narrow age range (McFarlane, Talerman & Steinberg, 1970; Williams & McFarlane, 1970; Salimonu *et al.*, 1978). However, Adeniyi and Ayeni (1976) reported plasma immunoglobulin levels in Nigerian infants in the first year of life. In the present work, a considerably larger number of subjects and of wider age range (1–50 years) were studied.

Materials and methods

A total of 703 blood samples were collected from people resident in Ibadan, Nigeria in February and March, 1980. This consisted of 411 male and 292 female participants. Most of the samples for the 1–5 year age group came from apparently normal children who reported for discharge following complete recovery from ailments which are not known to affect immune responses. They attended the children outpatient clinic of the University College Hospital (UCH), Ibadan. The rest of the samples for this age group were from normal children who showed up at Igbo-Ora for an ongoing medical research project. Samples for age groups 6–20 years were collected from volunteer students in one elementary and two secondary schools in Ibadan. The adult male blood samples were collected from the UCH, Ibadan blood donors. Most of the adult female samples were collected from hospital staff and their friends; a few samples came from female teachers and others from a few female patients showing up for clinical advice who were considered healthy. Twenty-three donors volunteered to be sampled for a repeat assay of the levels of their immunoglobulins during the rainy season — mid June.

About 2 ml of blood was collected by venepuncture from each child below 5 years of age, 5 ml from those above 5 years and 10 ml from individual adults. The blood samples were allowed to clot and retract in sterile universal bottles. The sera were separated into sterile bijou bottles which were immediately kept frozen at −20° C until needed.

Immunoglobulin levels were measured as previously described by Salimonu *et al.* (1978). The mean coefficient of variation for IgG was 6.16%. For IgA it was 16.13% while that for IgM was 16.95%.

Results

Tables 1–6 display the mean immunoglobulin concentrations and the range of normal values (mean ± 2 s.d.) in mg/100 ml for the different age groups surveyed.

Effect of age

In both males and females IgG increased inconsistently with advancing age up to 20 years. Thereafter the values reduced with further increase in age up to 40 years. The level rose again in the 41–50 year age group in both sexes. The differences were significant in all the age groups studied except in the 1–10 year age groups in the males and 31–50 year age groups in the females (Tables 1 and 2).

IgA rose with increasing age from 1 to 50 years in both sexes. The rise was inconsistent in the females and was consistent up to 30 years in the males. In the males, the differences were significant in all the age groups except in the 21–40 year age groups. In the females the differences were not significant in most age groups (Tables 3 and 4).

The IgM levels in the males rose inconsistently with increasing age up to the 41–50 year age

Table 1. Range of normal values for IgG in males in Ibadan

Age group (in years)	Mean (mg/100 ml)	s.d.	*n*	Normal range (mean ± 2 s.d.)
1–5	761	317.8	36	125–1397
6–10	668	200.2	54	268–1069
11–15	971	309.6	71	352–1590
16–20	1251	367.4	77	517–1986
21–30	907	310.0	74	287–1527
31–40	786	201.5	75	383–1189
41–50	957	219.4	24	518–1396

Table 2. Range of normal values for IgG in females in Ibadan

Age group (in years)	Mean (mg/100 ml)	s.d.	*n*	Normal range (mean ± 2 s.d.)
1–5	854	190.5	20	473–1235
6–10	997	343.4	58	310–1684
11–15	845	307.8	74	230–1461
16–20	1038	336.0	75	366–1710
21–30	911	331.0	45	249–1573
31–40	720	146.6	15	427–1013
41–50	740	218.0	5	304–1176

Table 3. Range of normal values for IgA in males in Ibadan.

Age group (in years)	Mean (mg/100 ml)	s.d.	*n*	Normal range (mean ± 2 s.d.)
1–5	81	34.5	36	12–150
6–10	110	36.5	54	37–183
11–15	141	54.1	71	33–249
16–20	162	51.8	77	58–265
21–30	187	82.1	74	22–351
31–40	172	58.6	75	55–290
41–50	211	57.9	24	95–326

Table 4. Range of normal values for IgA in females in Ibadan

Age group (in years)	Mean (mg/100 ml)	s.d.	*n*	Normal range (mean ± 2 s.d.)
1–5	90	40.7	20	8–171
6–10	141	56.3	58	29–254
11–15	154	54.5	74	45–263
16–20	153	57.1	75	39–268
21–30	186	51.1	45	84–288
31–40	177	65.3	15	46–307
41–50	206	65.6	5	75–337

group. The differences were significant in some age groups but were not in others. There was no significant elevation in IgM values with advancing age in the females (Tables 5 and 6).

Effect of sex

Females had higher levels of IgG up to the age of 10 years after which the male values became significantly higher up to the age of 20 years. There was no significant difference in the levels of IgG between the sexes after 20 years.

The level of IgA was higher in the females up to the age of 15 years. Thereafter males and females seem to have similar values. The sexual differences in IgA values were not statistically significant except in the 6–10 year age group.

IgM showed higher values in the females up to the 16–20 year age group. The differences were significant up to the age of 15 years. After 20 years of age, male values were consistently higher than female values. The differences were significant in the 21–40 year age groups.

Effect of season

Table 7 shows the mean concentrations of IgG, IgA and IgM for both dry and rainy seasons in the twenty-three individuals that were resampled. The range of values (mean ± 2 s.d.) for both seasons are also displayed.

Seven individuals had higher values of IgG in the dry season while sixteen had higher values in the rainy season. Higher IgA values were

Table 5. Range of normal values for IgM in males in Ibadan

Age group (in years)	Mean (mg/100 ml)	s.d.	*n*	Normal range (mean ± 2 s.d.)
1–5	75	21.4	36	33–118
6–10	65	20.7	54	24–107
11–15	92	27.9	71	36–147
16–20	100	57.0	77	0–214
21–30	124	61.7	74	1–247
31–40	122	55.3	75	12–233
41–50	132	56.3	24	19–244

Table 6. Range of normal values for IgM in females in Ibadan

Age group (in years)	Mean (mg/100 ml)	s.d.	*n*	Normal range (mean ± 2 s.d.)
1–5	98	33.2	20	31–164
6–10	96	52.7	58	0–201
11–15	111	45.0	74	21–201
16–20	114	48.1	75	18–211
21–30	105	37.3	45	30–179
31–40	96	32.5	15	31–161
41–50	103	43.4	5	16–190

Table 7. Immunoglobulin values obtained in the dry and rainy seasons

	Dry season				Rainy season					
Ig	Mean (mg/ 100 ml)	s.d.	*n*	Mean (± 2 s.d.)	Mean (mg/ 100 ml)	s.d.	*n*	Mean (± 2 s.d.)	*t*	*P*
IgG	943	316.7	23	309–1577	1087	235.6	23	615–1559	1.75	> 0.05
IgA	179	82.7	23	13–345	191	75.0	23	41– 341	0.51	> 0.2
IgM	115	46.7	23	21–209	117	57.6	23	2– 233	0.14	> 0.2

recorded in the dry season in eleven individuals and lower IgA values were recorded during the rainy season also in eleven individuals. One individual had the same level of IgA in both seasons. Twelve individuals had higher levels of IgM in the dry season while ten had higher levels in the rainy season. One individual had the same value for both seasons. None of the differences observed in the levels of IgG, IgA and IgM between the two seasons were statistically significant.

Test of homogeneity

In both sexes the Chi-square values obtained showed that both IgG and IgA were homogeneously distributed around their mean values regardless of age group ($P > 0.1$). IgM was heterogeneously distributed between the two age groupings (1–20 and 21–50 years) in both males and females ($P < 0.025$ and $P < 0.01$).

Discussion

There is quite a number of data on the normal levels of serum immunoglobulins in Ibadan, Nigeria (McFarlane & Voller, 1966; Williams & McFarlane, 1970; Ladipo, Salimonu & Osunkoya, 1978; Salimonu *et al.*, 1978). These are mainly control values limited to a few subjects and covering only a few age groups. However, Adeniyi and Ayeni (1976) have shown the plasma immunoglobulin levels in Nigerian in-

fants in the first year of life. In the present study, levels of immunoglobulins G, A and M were quantitated in 703 Nigerians aged between 1 and 50 years.

The decreasing IgG levels that we observed with rising age in adult Nigerians are consistent with the findings of Buckley and Dorsey (1970, 1971) in North Carolina. They however described a fall in mean concentrations of IgG only after the age of 35 years. The reason for the decrease in male IgG values in the 6–10 year age group and female IgG levels in the 11–15 year age group is not obvious. Stiehm and Fudenberg (1966) and Stoop *et al.* (1969) reported a decrease in IgG values between ages 12 and 16; and at age 12, respectively. Stoop *et al.* (1969) have suggested that this fall may be connected with the beginning of puberty.

It has been reported that boys are more susceptible to infections than girls (Childs, 1965). This difference in susceptibility may be responsible for the higher IgG levels observed in the males aged 11–20 years than their female counterparts. The lack of definite higher levels of IgG in favour of females above the age of 20 years could be due to the socio-economic class of the adult females sampled. This is probably why present findings differ slightly from those observed in Gambia by McGregor *et al.* (1970). They found IgG levels in females to be slightly but consistently higher than in males. Berg and Johansson (1969) working on samples obtained in Uppsala, Sweden found that girls (from 2 to 15 years of age) showed higher mean IgG concentrations than boys of similar ages. Differences due to sex rather than susceptibility to infection must have been responsible for the Swedish figures.

The present report has shown that serum IgA concentrations increased with advancing age. This supports the findings of other workers (Stoop *et al.*, 1969; Buckley & Dorsey, 1970, 1971). Our results also confirm the report of Berg and Johansson (1969) who observed that IgA levels had still not attained the adult level in the 13–15 year age group. Buckley and Dorsey (1970) have expressed the view that the fall in serum immunoglobulin concentrations with advancing age suggests an age-related abiotrophy of selected cells responsible for producing immunoglobulin molecules. They further suggested that the maintenance of concentrations of IgA suggests that this immunoglobulin may be of relatively greater importance with advancing age.

There was generally no significant difference in IgA levels between the two sexes. McGregor *et al.* (1970) also found no consistent difference in IgA values between the sexes in Gambia. Cassidy *et al.* (1974), working on sera obtained in a community health study in Tecumseh, Michigan from whites found significantly higher levels of IgA in males than in females. However, Stoop *et al.* (1969) reported IgA levels about the same in both sexes.

The general rise with increasing age observed for combined IgM values for both sexes, though insignificant, supports the findings of Mohammed, Tomkins and Greenwood (1973) in Zaria, Nigeria.

This work also confirms the observation of Berg and Johansson (1969) that the IgM in girls was higher than that in boys. The greatest difference was, however, found in the 6–10 year age group as opposed to 4 years in their own report. Grundbacher (1972) has suggested that the higher mean values for IgM in females support the hypothesis that the X chromosome of man carries genes with an effect on IgM concentration. Rhodes *et al.* (1969) obtained results supporting this suggestion.

The samples for the adult female groups (20–50 years) came from the middle and high classes of the society while their corresponding adult male samples cut across the socio-economic classes. It has been reported that standard of living (as an index of susceptibility to infection) can affect the levels of the immunoglobulins (Schofield, 1957; Buckley & Dorsey, 1971). This factor could therefore have contributed to the lower levels of the immunoglobulins found in adult females relative to their adult male counterparts.

The present study like most in the literature used cross-sectional analysis to identify trends which might be applicable to a single individual between the ages of 1 and 50 years. The results must be interpreted cautiously as longitudinal trends might differ considerably from cross-sectional analysis. There is evidence, however, that whole gamma-globulin concentrations increase progressively in individuals studied longitudinally between the ages of 4 and 20 years (Trevorrow, 1967).

The results obtained here differ from those of McFarlane (1966) who reported 2–3 times

higher values for IgG and IgM in the rainy season than in the dry season in Nigeria. His finding that IgA showed no definite seasonal variation was confirmed. In the present study the seasonal difference in IgG mean values was not statistically significant ($t = 1.75$, $P > 0.05$). This coupled with the fact that about one-third of the individuals examined gave higher IgG values in the dry season makes it difficult to attach any importance to the slight rise in mean value in the rainy season over the mean value obtained during the dry season. The difference in IgA mean values for both seasons was also not statistically significant ($t = 0.51$, $P > 0.2$). Variability in IgA values due to season could not be proved from our results as eleven individuals had higher levels in the dry season while eleven had higher levels in the rainy season. The IgM mean values for both seasons were not significantly different ($t = 0.14$, $P > 0.2$).

Present findings on effect of season on IgG, IgA and IgM levels confirm the report of other workers including McGregor *et al.* (1970) in Gambia and Stoop *et al.* (1969) in the Netherlands. Cornille-Brøgger, Mathews and Molineaux (1976) working in the Garki district of Kano State of Nigeria observed that the levels of IgM showed a seasonal variation similar in trend to that of *P. falciparum* parasitaemia. It could be said therefore that while no seasonal variation seems to affect normal levels of the immunoglobulins G, A, and M, it would be more difficult to select normal (infection-free) people in this environment during the rainy season than during the dry season.

It is difficult to believe that the variations obtained by McFarlane (1966) for IgG and IgM were due to seasonal effects, since he appeared to have sampled different groups of twenty-five Nigerians in the dry and rainy seasons. To further establish the effects of season on immunoglobulin levels in this environment, it will be necessary to sample a larger number of the same group of individuals towards the end of both seasons (March and October).

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