Is parental age a risk factor of mental retardation among their children?

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Background
Mental retardation is a condition of incomplete development of the mind, which is specially characterized by impairment of skills manifested during the development period, contributing to decrease the overall level of intelligence ICD-10.

Methodolgy
The study is an unmatched case–control study; the cases and controls were diagnosed according to the ICD-10 criteria, and the cases of mental retardation were subjected to psychometric assessment by using the Stanford Binet, version 4 or Vinland Maturity Scale. The controls were those with psychiatric disorders but were not mentally retarded.

Results
The highest percentage of mental retardation was the borderline type and the lowest was the severe type (30.2 and 2.7%, respectively). There was a significant odds ratio for the mothers of age group 30–34 years in the Vinland Maturity Scale group cases. In addition, there was a significant odds ratio for the fathers of age group above 50 years old, who were nine times more liable to have mentally retarded children.

Conclusion
There is a need for further studies of the risk factors for mental retardation among children, as our study results for this subgroup may be unique to a particular geographic area.

Keywords:
mental retardation, parental age, risk factors

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Introduction

Mental retardation (MR) is a condition of incomplete development of the mind, which is especially characterized by impairment of skills manifested during the development periods, contributing to decrease the overall level of intelligence ICD-10 [1]. Research findings have consistently shown a positive linear correlation between a mother's age at delivery and the child's measured mental ability [2,3]. In 2005, Malaspina and colleagues detected an 'inverted U-shaped relationship' between paternal age and intelligence quotients (IQs) in 44 175 people from Israel. There was a peak at paternal ages of 25–44 years; fathers younger than 25 and older than 44 tended to have children with lower IQs. They also reviewed the literature and found that at least half a dozen of other studies have demonstrated significant associations between paternal age and human intelligence.[4] Saha *et al*. [5] found that paternal age was associated with poorer scores in almost all neurocognitive tests used. Lopez-Castroman *et al*. [6] found that the average paternal age is elevated in cases of mental retardation. El Hazim *et al*. [7] found in the southern region in Kingdom of Saudi Arabia that the prevalence of mental retardation was estimated to be 8.2 per thousand.

MR is a long-life disorder for the children, causing severe distress to the parents and worrying about who will take care of them when the parent will be no more able to take care of them. Therefore, any effort done to find the risk factors associated with MR is highly appreciated. The result of this study will help develop awareness program for the secondary school students who will be the future parents.

Methodology

Study design

The design of the study is an unmatched case–control study.

Place of study

This study was conducted in Abha Psychiatric Hospital, which is a governmental hospital with 100 beds and giving service to one million and eight hundred thousand people of the southern region in the Kingdom of Saudi Arabia. There is a weekly outpatient clinic for boys until the age of 15 years and for girls until the age of 18 years. This clinic is held by two psychiatrists from King Khalid University.

Source of data

The data were collected by reviewing all the patients' records in the year 1432 Hijri of the child psychiatric clinics.

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Inclusion criteria

The inclusion criteria are as follows:

(1) Boys aged 15 years or below and girls aged 18 years or below were included in the study.
(2) Children whose medical records have contained all the following information were also included: parental age, psychometric assessment of intelligent quotient, or social maturity scale.

Exclusion criteria

The exclusion criteria were as follows:

(1) We excluded from the study any child whose medical record was missing one of the following covariates (parental age, psychometric assessment of either intelligent quotient, or social maturity scale for cases only).
(2) Those having no psychiatric illness or those aged above 18 years, or other nationality than Saudi, were also excluded.

Selection of cases and controls

The cases and controls were diagnosed according to the ICD-10 criteria; the cases were subdivided into two groups: those who have MR according to their IQ and those who have MR according to their social maturity quotient. We included in this study those who have an IQ below 90 or social quotient below 89 [measured by Stanford Binet, version 4 and Vineland maturity scale (VMS) (1989)]. The psychometric tests were administered individually by a psychometrist. The controls were those who have psychiatric disorders but are not mentally retarded. The total number of particpants was 187; we excluded the participants who have missing data (32), those who were above the age of 18 years (2), those without psychiatric illness (3), and other nationalities (3). There were 60 controls and 53 cases with IQ determined (IQ cases), and 34 cases with social maturity scale determined (VMS cases).

Statistical analysis

We used the odds ratios to assess the presence and strength of an association between paternal and maternal age at conception and MR. We used logistic regression modeling to obtain age-specific ratios adjusted simultaneously for the chosen covariates. The covariates are consanguinity, presence of congenital anomalies, presence of epilepsy, family history of mental retardation, birth order, sex, and incubation at birth.

Ethical consideration

The approval from the local medical ethics committee and the director of the hospital were obtained.

The data were introduced to the computer anonymously.

Results

Table 1 shows that the sex distribution is nearly equal in both IQ cases and controls (50.9 : 49.1 and 55 : 45), but in VMS cases the male to female ratio was 64.7 : 35.3.

As regards the birth order, the high birth order is almost the double of the low birth order in cases and controls.

As regards the years of education, 50% of the VMS cases did not go to school.

The maternal age was divided into four groups: below and equal to 19 years and equal and above 35 years, the two intermediate groups from 20 to 29 years and 30 to 34 years; we took the former as a reference group where the majority of cases and controls are present (47.2, 44.1, and 40).

As regards maternal education, there were missing data up to 62.3, 41.2, and 31.6% and illiteracy is the highest percent (13.2, 14.7, and 35%).

Maternal occupation, also similar to education, has a high percentage of missing data (62.3, 47.1, and 31.7%) and the majority were housewives (34, 47.1, and 63.3%).

Paternal age was divided into four groups: 30 years or less and above 50 years and the intermediate interval into two groups from 30 to 39 years and 40 to 49 years; the former was taken as the reference group where the majority lies (52.8, 38.2, and 45).

As regards paternal education, the missing data were the highest percent (35.8, 23.5, and 15%), and primary education was the highest in cases and controls (20.8, 29.4, and 33.3%).

As regards the paternal occupation also the missing data percentages were 49.1, 29.4, and 25%, and those who were jobless were 13.2, 5.9, and 18.3%.

As regards the severity of mental retardation in the IQ group (Table 2), the highest percentage was the borderline type and the lowest percentage was the severe type (30.2 and 2.7%), whereas in the VMS cases the highest percentage was the mild type and the lowest percentage was the severe type (10.9 and 1.4%).

The most frequent diagnosis in the IQ cases was enuresis (7.5%), in VMS cases it was overactive disorder with MR and stereotyped movement (26.9%), and in controls it was separation anxiety disorder (15%), as shown in Table 3.

Table 4 shows risk factors other than parental age, which are the congenital anomalies, birth order, consanguinity, epilepsy, sex of the child, incubation at birth, and family history of MR; all of them are nonsignificant for the IQ cases group, whereas for the VMS cases only the family history of MR was significant [odds ratio = 3.63, 95% confidence interval (CI) = 0.98–13.47, $P = 0.04$].

Table 5 shows the odds ratio for the association between parental age and MR in their children. There is a significant odds ratio for the mother's age group of 30–34 years in the VMS group cases (odds ratio = 4.89, 95%

Table 1 Background information of the studied sample

	n (%)		
Sample variable	IQ cases (*n*=53)	VMS cases (*n*=34)	Controls (*n*=60)
Child sex			
Male	27 (50.9)	22 (64.7)	33 (55)
Female	26 (49.1)	12 (35.3)	27 (45)
Birth order			
Low birth order	14 (26.4)	12 (35.3)	20 (33.3)
High birth order	39 (73.6)	22 (64.7)	40 (66.7)
Years of education			
0	9 (17)	17 (50)	19 (31.7)
1–3	29 (54.7)	11 (32.4)	18 (30)
4–6	7 (13.2)	3 (8.8)	14 (23.4)
7–9	1 (1.9)	2 (5.9)	9 (14.9)
Missing data	7 (13.2)	1 (2.9)	
Maternal age			
≤19	7 (13.2)	3 (8.8)	4 (6.7)
20–29	25 (47.2)	15 (44.1)	40 (66.6)
30–34	13 (24.5)	11 (32.4)	6 (10)
≥35	8 (15.1)	5 (14.7)	10 (16.7)
Maternal education			
Graduated	1 (1.9)	2 (5.9)	1 (1.7)
Secondary	3 (5.7)	3 (8.8)	4 (6.7)
Intermediate	4 (7.5)	1 (2.9)	3 (5.0)
Primary	3 (5.7)	6 (17.6)	10 (16.7)
Read and write	2 (3.8)	3 (8.8)	2 (3.3)
Illiterate	7 (13.2)	5 (14.7)	21 (35)
Missing	33 (62.3)	14 (41.2)	19 (31.6)
Maternal occupation			
Housewife	18 (34)	16 (47.1)	38 (63.3)
Clerk	2 (3.8)	2 (5.8)	2 (3.4)
Retired			1 (1.7)
Missing data	33 (62.2)	16 (47.1)	19 (31.6)
Paternal age			
<30	13 (24.5)	6 (17.7)	19 (31.6)
30–39	28 (52.8)	13 (38.2)	27 (45)
40–49	7 (13.2)	6 (17.7)	12 (20)
≥50	5 (9.5)	9 (26.4)	2 (3.4)
Paternal education			
Graduate	2 (3.8)	1 (2.9)	3 (5)
Secondary	7 (13.2)	5 (14.7)	5 (8.3)
Intermediate	6 (11.3)		7 (11.7)
Primary	11 (20.8)	10 (29.4)	20 (33.3)
Read and write	3 (5.7)	3 (8.8)	5 (8.3)
Illiterate	5 (9.4)	7 (20.6)	11 (18.3)
Missing data	19 (35.8)	8 (23.5)	9 (15)
Paternal occupation			
Jobless	7 (13.2)	2 (5.9)	11 (18.3)
Soldier/seller	7 (13.2)	10 (29.4)	18 (30)
Clerk	12 (22.6)	7 (20.6)	10 (16.7)
Farmer		1 (2.9)	1 (1.7)
Student			1 (1.7)
Retired	1 (1.9)	4 (11.8)	4 (6.7)
Missing data	26 (49.1)	10 (29.4)	15 (25)

IQ, intelligence quotient; VMS, Vinland Maturity Scale.

CI = 1.54–15.57, $P = 0.008$), which means that mothers who are aged 30–34 years are five times more liable to give birth to mentally retarded children compared with the younger age group.

There is a significant odds ratio for the father's age group equal to and above 50 years (odds ratio = 9.35, 95% CI = 1.76–49.6, $P = 0.005$), which means that fathers who are above 50 years old are nine times more liable to have mentally retarded children compared with who are less than this age.

However, when we adjusted the odds ratio of all variables, the mother's age becomes insignificant, and only the father's age, as well as the family history of MR, became more significant. Those fathers who are older than 50 are 20 times more liable to have mentally retarded children than those who are less than 50 (odds ratio = 20.21, 95% CI = 1.97–207.61, $P = 0.01$).

Those who have family history of MR are eight times more liable to have MR than those who have no family history of MR (odds ratio = 7.99, 95% CI = 1.32–39.31, $P = 0.02$).

Discussion

The incidence of MR is elevated when children are born to older parents [8,9], such as the incidence of Down's syndrome [10], schizophrenia [11], and behavioral problems [12].

Many other health conditions also are related to parental age. Older mothers are more likely to have children with intellectual disabilities generally, partly through increased risk of low birth weight [13].

Because the trend of increasing rates of MR coincides with rising paternal age at birth, recent research suggests increased de novo mutations in men's sperm, as age may play a role in this trend [14,15]. Most research about maternal age focuses on health during pregnancy and delivery, finding that older mothers are more likely to have pre-eclampsia, stillbirths, and adverse perinatal outcomes [13,16].

Using a broad measure of disability, and considering mothers' and fathers' ages together, these results show that maternal age is much more strongly associated with children's cognitive disability. The results for paternal age are not consistent with the suggestion that de novo mutations in older men increase the risk of conditions such as autism spectrum disorder that may be triggered by such mutations [14].

Table 2 Severity of mental retardation

	n (%)	
Categories	IQ group (*n*=53)	VMS group (*n*=34)
Borderline	16 (30.2)	8 (23.5)
Mild	18 (34)	16 (47)
Moderate	15 (28.3)	8 (23.5)
Severe	4 (7.5)	2 (6)
Total	53 (100)	34 (100)

IQ, intelligence quotient; VMS, Vinland Maturity Scale.

Table 4 Risk factors in cases and controls

	n (%)			
Factors	IQ cases (*n*=53)	VMS cases (*n*=34)	Controls (*n*=60)	*P*
Congenital anomalies				
Present	10 (18.9)	6 (17.6)	5 (8.3)	NS
Absent	43 (81.1)	28 (82.4)	55 (91.7)	
Birth order				
Low	14 (26.4)	12 (35.3)	20 (33.3)	NS
High	39 (73.6)	22 (64.7)	40 (66.7)	
Consanguinity				
Present	25 (47.2)	14 (41.2)	20 (33.3)	NS
Absent	28 (52.8)	20 (58.8)	40 (66.7)	
Epilepsy				
Present	8 (15.1)	6 (17.6)	7 (11.7)	NS
Absent	45 (84.9)	28 (82.4)	53 (88.3)	
Sex of the child				
Male	27 (50.9)	22 (64.7)	33 (55)	NS
Female	26 (49.1)	12 (35.3)	27 (45)	
Incubation after birth				
Present	6 (11.3)	6 (17.6)	5 (8.3)	NS
Absent	47 (88.7)	28 (82.4)	55 (91.7)	
Family history of MR[a]				
Present	6 (11.3)	7 (20.6)	4 (6.7)	0.04
Absent	47 (88.7)	27 (79.4)	56 (93.3)	

CI, confidence interval; IQ, intelligence quotient; MR, mental retardation; VMS, Vinland Maturity Scale.
[a]Odds ratio=3.63, 95% CI=0.98–13.47.

Table 3 Frequency of the Sample diagnoses

		n (%)		
Diagnosis	ICD-10	IQ cases (*n*=53)	VMS cases (*n*=34)	Controls (*n*=60)
Separation anxiety	F93.0	1 (1.9)	1 (2.9)	9 (15)
Disturbance of activity and attention	F90.0	1 (1.9)	1 (2.9)	7 (11.7)
Enuresis	F98.0	4 (7.5)	0 (0.0)	6 (10)
Reaction to severe stress	F43	1 (1.9)	0 (0.0)	5 (8.3)
Socialized conduct disorder	F91.2	0 (0.0)	0 (0.0)	3 (5.0)
Phobic anxiety disorder	F93.1	3 (5.7)	2 (5.9)	3 (5.0)
Epilepsy	G40	1 (1.9)	2 (5.9)	3 (5.0)
Other emotional disorder	F93.8	1 (1.9)	0 (0.0)	2 (3.3)
Sleep disorder	F51	0 (0.0)	0 (0.0)	2 (3.3)
Transient tic disorder	F95.0	0 (0.0)	0 (0.0)	2 (3.3)
Sibling rivalry	F93.3	1 (1.9)	1 (2.9)	2 (3.3)
Unspecified disorder of psychol. development	F80.9	0 (0.0)	0 (0.0)	1 (1.7)
Oppositional defiant disorder	F91.3	0 (0.0)	0 (0.0)	1 (1.7)
Stereotyped movement disorder	F98.4	0 (0.0)	0 (0.0)	1 (1.7)
Depressive conduct disorder	F92.0	1 (1.9)	0 (0.0)	1 (1.7)
Asperger	F84.5	0 (0.0)	0 (0.0)	1 (1.7)
Obsessive compulsive disorder	F42	1 (1.9)	0 (0.0)	1 (1.7)
Manic depressive disorder	F32	0 (0.0)	0 (0.0)	1 (1.7)
Specific speech and articulation disorder	F80.0	1 (1.9)	1 (2.9)	1 (1.7)
Trichotillomania	F63.3	1 (1.9)	0 (0.0)	1 (1.7)
Dissociative disorder	F44	0 (0.0)	0 (0.0)	1 (1.7)
Autism	F84.0	0 (0.0)	0 (0.0)	1 (1.7)
Socialized conduct disorder + enuresis	F91.2 + 98	0 (0.0)	0 (0.0)	1 (1.7)
Epilepsy + enuresis	G40 + 98	0 (0.0)	0 (0.0)	1 (1.7)
Other emotional disorder + enuresis	F93.8 + 98	0 (0.0)	0 (0.0)	1 (1.7)
Kleptomania + enuresis	F63 + 98	0 (0.0)	0 (0.0)	1 (1.7)
Phobic anxiety disorder + encorpresis	F93.1 + 98.1	0 (0.0)	0 (0.0)	1 (1.7)
Stuttering		1 (1.9)	1 (2.9)	0 (0.0)
Overactive disorder with MR and stereotyped movement	F84.4	0 (0.0)	9 (26.9)	0 (0.0)
Unspecified pervasive developmental disorder	F84.9	0 (0.0)	1 (2.9)	0 (0.0)
Other pervasive developmental disorder	F84.3	1 (1.9)	0 (0.0)	0 (0.0)
Only mental retardation	F70–79	34 (64.2)	15 (44.1)	0 (0.0)
Total		53 (100)	34 (100)	60 (100)

IQ, intelligence quotient; MR, mental retardation; VMS, Vinland Maturity Scale.

Table 5 Odds ratio for the association between parental age and mental retardation in their children

	IQ cases				VMS cases			
Parental age	Case ($n=53$)	Control ($n=60$)	Odds ratio	95% CI	Case ($n=34$)	Control ($n=60$)	Odds ratio	95% CI
Maternal age								
≤19	7	4	0.36	0.09–1.35	3	4	0.50	0.10–2.50
20–29[a]	25	40			15	40		
30–34**	13	6	3.45	1.17–10.3	11	6	4.89	1.54–15.57
≥35	8	10	1.28	0.45–3.68	5	10	1.33	0.39–4.55
Paternal age								
<30	13	19	1.52	0.63–3.66	6	19	1.53	0.49–4.73
30–39[a]	28	27			13	27		
40–49	7	12	0.56	0.19–1.64	6	12	1.04	0.32–3.39
≥50***	5	2	2.41	0.43–13.50	9	2	9.35	1.76–49.60

CI, confidence interval; IQ, intelligence quotient; VMS, Vinland Maturity Scale.
[a]Reference group.
**$P=0.008$.
***$P=0.005$.

Maternal age (but not paternal age) affects children partly because it is associated with the mother's health (which declines at older ages) at the time of pregnancy and delivery [17].

A surprising finding in this study was the markedly higher-than-expected prevalence of MR among children whose fathers were more than 50 years of age after we controlled for other competing factors.

Table 1 shows that the sex distribution is nearly equal in both IQ cases and controls (50.9 : 49.1 and 55 : 45), but in VMS cases the male to female ratio is 64.7 : 35.3. As regards the birth order, the high birth order is almost the double of the low birth order in cases and controls.

As regards years of education, 50% of the VMS cases did not go to school.

Maternal age was divided into four groups: 19 years and younger and 35 years and older, the two intermediate groups from 20 to 29 and 30 to 34; we took the former as a reference group where the majority of cases and controls are present (47.2, 44.1, and 40).

In the study by Champan *et al.* [18], the predictive value of maternal age and education in relation to rates of administratively defined MR in a 3-year birth cohort ($N = 267\,277$) was studied. Low maternal education placed individuals at an increased risk for both educable mentally handicapped and trainable mentally handicapped placements. Older maternal age was associated with increased risk of MR, but for individuals with educable mentally handicapped this age effect was only seen in the lowest education group. In terms of population-level risk, it was younger mothers with 12 years of education or less whose births were associated with the greatest proportion of MR. From a public policy viewpoint, children born to mothers with low levels of education are an important group to target for prevention/early intervention efforts.

In one of the first Atlanta Study publications, Drews *et al.* [19] analyzed 458 10-year-old children with MR and 563 comparison children from the Atlanta Study project data. Low maternal education, low socioeconomic status, and Black race were associated with mild but not severe MR.

Croen *et al.* [20] identified 16 735 children with MR of no known cause from California Department of Developmental Services records. Male sex, low birth weight, Black race, older maternal age, and low maternal education were associated with an increased risk for both mild and severe MR.

Chapman *et al.* [18] investigated the effect of maternal education and maternal age on risk for mild and moderate/severe MR identified through public school records. Older maternal age was associated with an increased risk for both levels of MR, but maternal education over 12 years reduced the risk for mild and moderate/severe MR by a factor of 15 and 4, respectively, compared with women with less than 12 years of education.

The paternal age was divided into four groups: 30 years or less and above 50 years and the intermediate interval into two groups from 30 to 39 and 40 to 49; the former was taken as the reference group where the majority lies (52.8, 38.2, and 45).

As regards paternal education, the missing data were the highest percent (35.8, 23.5, and 15%) and primary education was the highest in cases and controls (20.8, 29.4, and 33.3%).

As regards paternal occupation also the missing data percentages were 49.1, 29.4, and 25%, and the percentages who were jobless were 13.2, 5.9, and 18.3%.

Prasad *et al.* [21] reported that 63.3% of the parents of the mentally retarded children have age more than 41 years and 30% of parents are illiterate, 20% had primary education, and 20% had high education; as regards their occupation, 3.3% were jobless, 30% were employed, and 23.3% were businessmen.

A study conducted by Malaspina *et al.* in [22] showed a significant inverted u-shaped relationship between paternal age and IQ scores, which was independent from a similar association of IQ scores with maternal age. These relationships were not significantly attenuated by controlling for multiple possible confounding factors, including the other parent's age, parental education, social class, sex and birth order, birth weight, and birth complications. Overall, parental age accounted for ∼2% of the total

variance in IQ scores, with later paternal age lowering nonverbal IQ scores more than verbal IQ scores.

As regards the severity of MR in the IQ group (Table 2), the highest percent was the borderline type and the lowest was the severe type (30.2 and 2.7%), whereas in the VMS cases the highest percentage was the mild type and the lowest was the severe type (10.9 and 1.4%).

The most frequent diagnosis in the IQ cases was enuresis (7.5%), in VMS cases it was the overactive disorder with MR and stereotyped movement (26.9%), and in controls it was the separation anxiety disorder (15%), as shown in Table 3.

Floares [23] reported that handicapped patients with mental and neurological disability may have nocturnal enuresis, coexisting with day-time incontinence, sometimes both urinary and fecal (50–60% in our unit). Dekker and Koot [24] found a prevalence of 14.8% for attention-deficit hyperactivity disorder in Dutch children attending special schools, and Emerson [25] reported rates of 8.7% for hyperkinetic disorder in children with global learning disability, representing a 10-fold increased risk compared with the prevalence of hyperactivity (0.9%) in the general population sample.

Table 4 shows risk factors other than the parental age, which are congenital anomalies, birth order, consanguinity, epilepsy, sex of the child, incubation at birth, and family history of MR; all of them are nonsignificant for the IQ cases group, whereas for VMS cases only the family history of MR was significant (odds ratio = 3.63, 95% CI = 0.98–13.47, $P = 0.04$).

In the study by Croen *et al.* [26], mild MR was observed for boys, low birth weight children, multiple births, second-born or later-born children, and children whose mothers were 30 or more years of age at delivery, had less than a high school education, were born outside of California, or were Black.

Table 5 shows the odds ratio for the association between parental age and MR in their children. There is a significant odds ratio for the mother's age group of 30–34 years in the VMS group cases (odds ratio = 4.89, 95% CI = 1.54–15.57, $P = 0.008$), which means that mothers who are aged 30–34 years are five times more liable to give birth to mentally retarded children than the younger age group.

There was a significant odds ratio for the father's age group equal to and above 50 years (odds ratio = 9.35, 95% CI = 1.76–49.6, $P = 0.005$), which means that fathers who are above 50 years old are nine times more liable to have mentally retarded children compared with those who are less than this age.

However, when we adjusted the odds ratio of all variables, mother's age became insignificant, and only the father's age, as well as the family history of MR, became more significant. Those fathers who are older than 50 are 20 times more liable to have mentally retarded children than those who are less than 50 (odds ratio = 20.21, 95% CI = 1.97–207.61, $P = 0.01$). There is only weak positive correlation between the mother's age and the IQ in the IQ cases group, but not in the VMS cases group.

A study conducted by Williams and Decoufle [27] showed markedly elevated risk of codevelopmental retardation among Black children of mothers aged 30 years or more that was not attributable to Down's syndrome. A modest increase in risk for codevelopmental retardation was observed among white children born to older mothers, but it was entirely due to Down's syndrome.

Conclusion

We believe that there is a need for further study of the risks for MR among children, as our results for this subgroup may be unique to a particular geographic area or birth cohort.

Conflicts of interest

There are no conflicts of interest.

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